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Science

Conserving Biodiversity

AAAS

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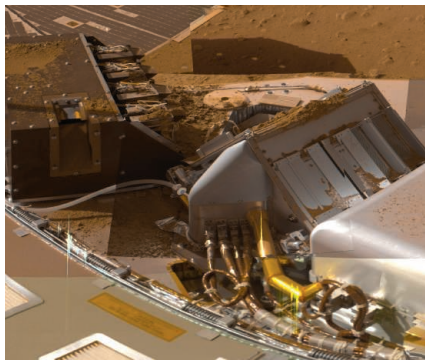

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COVER

Seeds in storage containers destined for the Millennium Seed Bank, a conservation project run by Kew Gardens, UK, which now houses 10 percent of the world's plant species as seeds. The conservation of biodiversity is in the spotlight as scientists, nongovernmental organizations, and politicians prepare for the Convention on Biological Diversity in Nagoya, Japan, in October 2010. See the special News Focus section beginning on page 1272 and the Review on page 1298.

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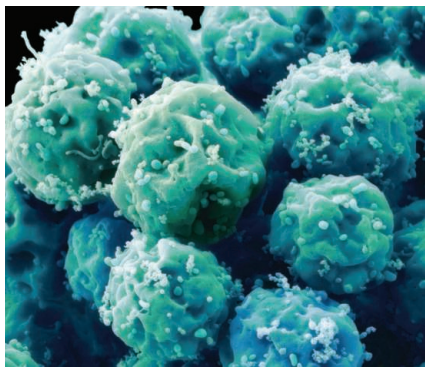

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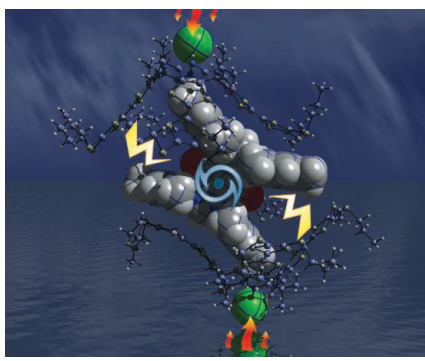

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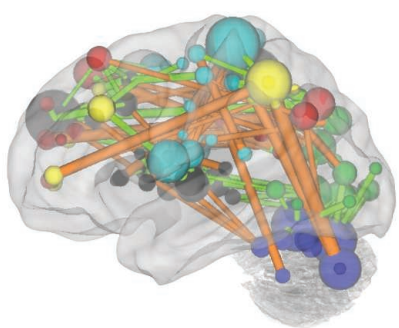

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Bruce Alberts is Editor-in-Chief of *Science*.

Overbuilding Research Capacity

POLICIES THAT OFFER INCENTIVES FOR INDIVIDUALS AND INSTITUTIONS CAN UNINTENTIONALLY induce harmful behaviors. One such perverse incentive encourages U.S. universities, medical centers, and other research institutions to expand their research capacities indefinitely through funds derived from National Institutes of Health (NIH) research grants. A reliance on the NIH to pay not only the salaries of scientists but also the overhead (or indirect) costs of building construction and maintenance has become a way of life at many U.S. research institutions, with potential painful consequences. The current trajectory is unsustainable, threatening to produce a glut of laboratory facilities reminiscent of the real estate bust of 2008 and, worse, a host of exhausted scientists with no means of support.

The NIH actually rewards institutions for paying faculty salaries with unguaranteed "soft money" from research grants by providing increased overhead payments. Amazingly, any institution that draws on its own finances to pay its professors is doubly disadvantaged: It must not only use its own funds but also loses the overhead on the salaries that it would otherwise accrue. In addition, the NIH will reimburse institutions for the cost of new research buildings, paid out as overhead charges on research grants as the building depreciates over several decades. The possibility that the NIH will ultimately pay for both new building costs and new staff enables the many advocates for expansion to effectively argue that the costs will eventually be borne in large part by the U.S. government.

This type of argument has strongly encouraged a large number of institutions to expand "on spec," taking out loans and gambling that they will win enough NIH research grants to pay for the expansion. There is a huge risk here. Because the NIH budget cannot increase at a high enough rate to pay for the ever-expanding U.S. biomedical research enterprise, each institution is betting that the faculty in its new facilities will outcompete those at other institutions for the limited research grants available. Institutions are thus pitted against each other in a process that resembles an arms race.

The results are not pretty. With success rates for acquiring an NIH grant below 10% in some cases, achieving a stable research career now has elements of a lottery, with one's future depending on a chance ranking assigned through a peer-review process that is unable to discriminate adequately among a sea of research proposals. Biomedical scientists are spending far too much effort writing grant applications and reviewing those of others, leaving precious little time to do what they should be doing: reading the scientific literature and thinking deeply about their research and teaching. And I worry about the future of universities, given the incentives to overinvest in research at the expense of needed facilities and faculty for teaching.

What can be done? NIH Director Francis Collins has boldly stated that "it is time for NIH to develop better models to guide decisions about the optimum size and nature of the U.S. workforce for biomedical research."* I agree. One possibility is for the NIH to require that at least half of the salary of each principal investigator be paid by his or her institution, phasing in this requirement gradually over the next decade. Alternatively, the maximum amount of money that the NIH contributes to the salary of research faculty (its salary cap) could be sharply reduced over time, and/or an overhead cost penalty could be introduced in proportion to an institution's fraction of soft-money positions (replacing the overhead cost bonus that currently exists).

Regardless of mechanism, here is my bottom line: A new NIH policy must make it unambiguously clear that expansion through laboratory building construction requires a substantial, nonreimbursable, long-term commitment of resources, including "hard-money" faculty support, by any institution that wants to increase its facilities and research staff. Although change will be painful, it is urgently needed to maintain a healthy biomedical research enterprise.

– Bruce Alberts

10.1126/science.1197077

*F. S. Collins, *Science* **327**, 36 (2010).

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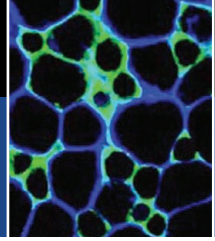

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HIGH-ENERGY PHYSICS

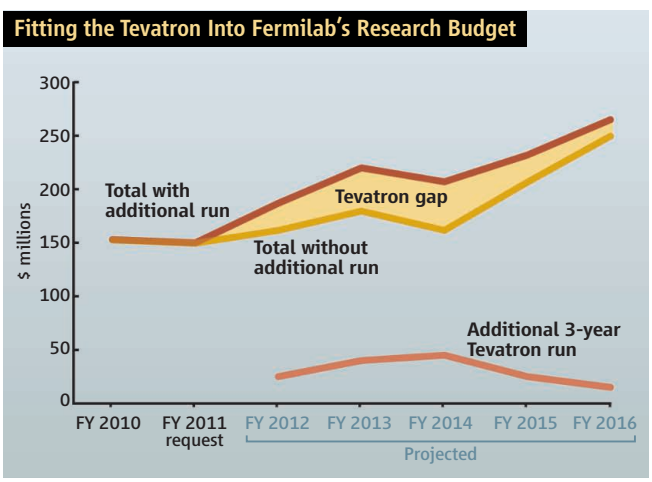
Higgs or Bust? Fermilab Weighs Adding 3 Years to Tevatron Run

Scientists at the last remaining U.S. particle physics lab have a shot at a major discovery. But pursuing that prize means delaying other projects that could enhance the lab's long-term viability. Should they still go for the glory?

That's the question facing Pier Oddone, director of Fermi National Accelerator Laboratory (Fermilab) in Batavia, Illinois. Last week, an independent advisory committee urged him to run the lab's 25-year-old atom smasher, the Tevatron collider, for an additional 3 years through 2014. The extension would give Fermilab researchers a chance to beat their European rivals in spotting the most prized particle in physics, the Higgs boson. That chance, the panel concluded, is worth potential disruption in the schedules of other projects. Unfortunately for Oddone, however, it could also cause problems for the U.S. Department of Energy (DOE), which funds the lab, and jeopardize the lab's future.

The Higgs boson is the lynchpin to physicists' explanation of how all particles get their mass. And Fermilab researchers have a chance to see it first because the more-powerful Large Hadron Collider (LHC) at the European particle physics laboratory, CERN, near Geneva, Switzerland, is running years behind schedule. In February, CERN announced that the collider will shut down for extensive repairs for at least 15 months beginning in 2012. At that point, the LHC won't have produced enough data to surpass the Tevatron in the race for the Higgs.

"This opportunity just dropped into our laps, and it's too good to pass up," says JoAnne Hewett, a theorist at SLAC National Accelerator Laboratory in Menlo Park, California, and a member of Fermilab's Physics Advisory Committee. The 15-person committee felt so strongly that it urged Oddone to extend the Tevatron's run past the scheduled September 2011 shutdown even if the lab doesn't receive extra money to pay for it.



On the spot. Fermilab Director Pier Oddone faces tough budget choices if he doesn't shut down the Tevatron next year.

GRAPH SOURCE: JEFFREY APPEL/FERMI NATIONAL ACCELERATOR LABORATORY; REIDAR HAHN/FERMILAB

Plenty of other prominent physicists would like to see Fermilab go for it. "The best long-range plan for Fermilab is to find the Higgs boson," says John Marburger, vice president for research at Stony Brook University in New York state. Marburger was science adviser to President George W. Bush after serving as director of DOE's Brookhaven National Laboratory in Upton, New York.

Other observers, however, say the committee's advice ignores fiscal realities. "You often get one of these [recommendations] where you say, 'Thank you very much, but there's nothing I can do with this,' " says William Madia, vice president for SLAC at Stanford University. Madia, a former head of two DOE national labs, says lab directors often have to take a committee's advice "with a grain of salt."

The recommendation to continue the Tevatron does not enjoy universal support even at Fermilab, which would risk losing ground to competitors if it slowed work on other projects. "We're not thrilled about it," says Mark Messier, an experimenter at Fermilab and co-spokesperson for a $260 million experiment currently under construction called NOνA. NOνA, which aims to start taking data in earnest in 2013, will study particles called neutrinos. Physicists generate the neutrinos by firing protons into a carbon target, and running the Tevatron would drain away 40% of those protons. If the Tevatron keeps running, Messier says, then "when other experiments that are competitive with NOνA come online, we'll have [only] half of the planned data set."

DOE officials may not be eager to change course, either. Anticipating that the LHC would soon eclipse the Tevatron as the world's highest-energy collider, Fermilab officials sought support for a multibillion-dollar particle smasher called the International Linear Collider (ILC) that would complement the LHC. But in February 2007, DOE warned U.S. physicists that the ILC could not be built until the mid-2020s and asked the community for alternatives. The consensus was to redirect Fermilab from the "energy frontier," where scientists search for massive new particles like the Higgs, to the "intensity frontier," where they use high-intensity proton beams like NOνA's to study neutrinos and other familiar particles in great detail.

Observers say that any change in direction now would be tricky for Dennis Kovar, DOE's associate director for high-energy physics, who argued for a half-dozen projects in Fermilab's new plan. In fact, the NOνA project received $55 million last year in the $787 billion federal stimulus package, which backed "shovel ready" projects of surpassing scientific importance. "If [Oddone] goes ahead and says, 'I'll run the Tevatron longer,' he's saying this [future] program isn't as interesting as he thought," says Nicholas Samios, who served as Brookhaven's director from 1982 to 1997. "And that's where Kovar may have a problem."

Money is also a problem. Running the Tevatron for three more years would cost $150 mil-

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lion. Scrounging that much cash from DOE's $810 million annual high-energy physics budget would be tough. Taking it from other programs funded by DOE's $4.9 billion science budget could be tougher. Still, the proposal has a chance. "We're taking it very seriously and considering all our options," says William Brinkman, director of DOE's Office of Science. Where the money might come from is "totally uncertain at this point," he says.

Even the scientific argument for continuing the Tevatron's run is subtle. If the Tevatron runs through 2014, physicists working with the two big experiments it feeds would collect enough data to see strong signs of the Higgs but not enough to clinch a definite discovery. Nevertheless, 38 leading theorists, including four Nobel laureates, found that prospect so tantalizing that on 28 July they sent a letter to Energy Secretary Steven Chu, himself a Nobel Prize–winning physicist, urging him to push for the extension.

Unfortunately for Oddone, that letter didn't come with a check. "If there is no additional funding, then it could very well be that, in the end, my decision will be not to proceed with running the Tevatron," he warns. A decision should come within weeks. DOE and other federal agencies will soon be sending their 2012 budget requests to the White House for the fiscal year that begins in October 2011. And lab officials say that budget mavens will probably insist that the fate of the Tevatron be spelled out as part of DOE's submission.

–ADRIAN CHO

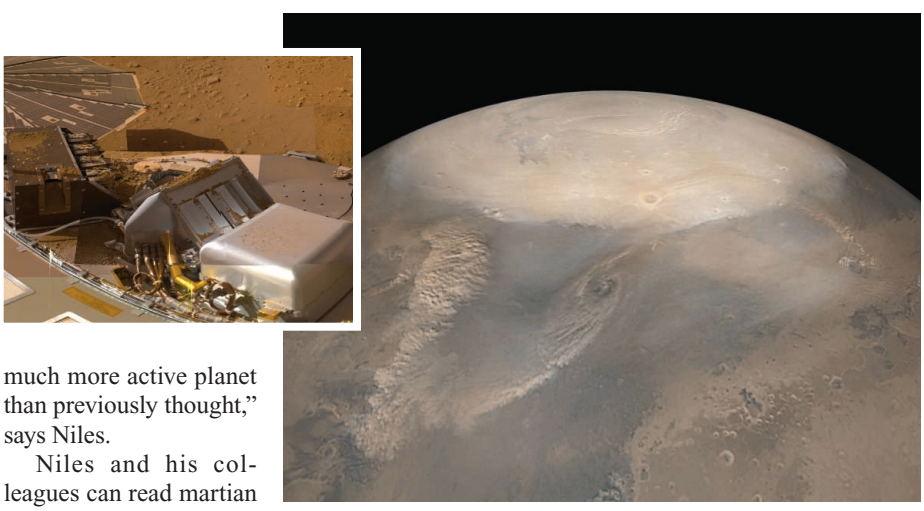
PLANETARY SCIENCE

Phoenix Lander Revealing a Younger, Livelier Mars

Brave little Phoenix keeps on giving. Although the ice of a deeply frigid martian winter wrecked the lander last year, data it returned in 2008 are yielding signs that Mars has been surprisingly lively these past few billion years, at least in a geochemical sort of way. Phoenix's measurements of the isotopic composition of atmospheric carbon dioxide are pointing to an atmosphere rejuvenated by volcanic outpourings, possibly up to the very recent geologic past. Moreover, despite what looks like eons of frigid dryness, the atmosphere may have been chemically interacting with liquid water recently. And where there's liquid water, of course, there could be life.

The new isotopic analyses "may be one of the most profound results from Phoenix," says planetary scientist Bruce Jakosky of the University of Colorado, Boulder, who is not on the Phoenix team. He does warn, however, that controversy will dog these Phoenix results.

In this week's issue of *Science* (p. 1334), planetary scientist Paul Niles of NASA's Johnson Space Center in Houston, Texas, and his colleagues report atmospheric isotopic measurements by Phoenix's mass spectrometer. The measurements have uncertainties that are one-tenth those of the only other such measurements, those from the two Viking landers in the 1970s. To the scientists' surprise, the sharper picture reveals that the isotopic composition of the carbon dioxide on a cold, dry, volcanically quiescent planet is quite similar to that of carbon dioxide on warm, wet Earth, where volcanoes erupt every day. One way or another, "Mars is a much more active planet than previously thought," says Niles.



Target Mars CO_2. A Phoenix lander instrument (*inset*) measured isotopes in CO_2, which freezes across the north pole in winter.

Niles and his colleagues can read martian history in the proportion of heavy isotope to light isotope in both the carbon and the oxygen of carbon dioxide because various geochemical processes leave their mark on carbon dioxide's isotopic composition. For example, back in Mars's early days when the then-fierce solar wind ate away at the atmosphere, it preferentially removed the lighter, more easily eroded carbon isotope—carbon-12—and left heavier carbon-13 behind. But the Phoenix measurements show that current atmospheric carbon is lighter than expected.

The implication, says Niles, is that "the last billion to 500 million years, Mars had active degassing of volcanic carbon dioxide." Erupting volcanoes would contribute carbon dioxide from the rocky interior whose carbon is isotopically lighter. No currently active volcanoes are known on Mars, but geologists have seen lava fields dating from as recently as the past 100 million years or so.

However, Niles and his colleagues did not see a volcanic signal in Phoenix's oxygen isotopic composition, so they infer that carbon dioxide has been interacting with liquid water on Mars. If the atmosphere were to react with water and rock to form carbonate minerals, atmospheric oxygen would become lighter because the heavier isotope reacts more readily. That would preferentially remove the heavier oxygen isotope from the atmosphere and negate the volcanic signal.

Interaction with liquid water could be "happening on modern Mars or in the fairly recent geologic past," says Niles. Support-

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ing evidence comes from meteorites blasted off Mars that landed on Earth. The carbonates in these meteorites have similar isotopic compositions to those of the modern martian atmosphere. One problem: There's plenty of water ice, but no liquid water is known on Mars today. Niles says the culprit could have been meltwater that might form every 100,000 years or so during martian warm spells, water that has briefly gushed down crater walls to form gullies in the geologically recent past, or even thin films of water or brine on dust particles or in martian soil today. Any of these could be at least a temporary abode for life.

The Phoenix atmospheric isotopes will generate some controversy, says Jakosky. "Their conclusion about the importance of [volcanic] outgassing is probably correct," he says, but atmospheric interaction with liquid water "is a plausible interpretation, not a unique one. The problem is there are many components in the [isotopic] system. On the basis of limited data, it's hard to point to one as the driving process."

Geochemist John Eiler of the California Institute of Technology in Pasadena agrees about the complexity and adds that carbonates in martian meteorites aren't good for comparison; some probably formed on Earth, not Mars, he says. But help is on the way. The Mars Science Laboratory, now dubbed Curiosity, is scheduled to land on Mars in 2012 with a mass spectrometer to determine both atmospheric and mineral isotopes.

–RICHARD A. KERR

ScienceNOW

From *Science*'s Online Daily News Site

Solid Gold, Thanks to Bacteria

Treasure hunters may have an unexpected ally in bacteria. The secret lies in a thin layer of microbes, known as a biofilm, that researchers found enveloping gold grains in a Queensland mine. The biofilm dissolves the gold on contact, creating toxic gold ions that can break down the bacteria's cell walls. But the bacteria fight back by transforming the ions into metallic gold nanoparticles that later coalesce into lacelike crystals across the surface. This form of gold is much purer than the original gold grains, which also contain silver and mercury, and is thus much more attractive to miners, the team reports in *Geology*. The researchers speculate that if they could genetically modify the bacteria to fluoresce when they purify the gold, the bugs could become something even more important: microbial metal detectors. http://bit.ly/solid-gold

Eek! An Ant!

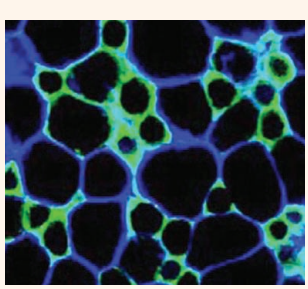
A nose full of biting ants can really spoil your appetite. Especially if your nose is 3 meters long. A new study reveals that African bush elephants avoid acacia trees that house swarming ant colonies—and preserve the surrounding landscape in the process.

Whistling thorn trees bristle with the 5-centimeter-long thorns typical of many acacias, but some of the spikes also swell into hollow bulbs the size of Ping-Pong balls. Crematogaster ants colonize the empty thorns and feed on nectar secreted from the plant's leaves. Ecologists Todd Palmer of the University of Florida, Gainesville, and Jacob Goheen of the University of Wyoming in Laramie found that elephants avoided eating the branches from these trees, or any other branches that the researchers placed the ants on.

The aversion has a visible effect on the entire African savanna. On sandy soil, where whistling thorn trees can't grow, elephants devastate trees, just as ecologists always expected. But on clay soils, where whistling thorn thrives, satellite images show that the trees flourish whether elephants are present or not, the team reports in *Current Biology*. "These little tiny ants are making a difference we can see from outer space," Goheen says. http://bit.ly/tree-ants

How Fish Oil Fights Inflammation

Pass the bass, please. Omega-3 fatty acids, a main component of fish oil, have a reputation as potent anti-inflammatory agents. Now researchers think they know how the acids block this immune response.



Jerrold Olefsky, an endocrinologist at the University of California, San Diego, and colleagues found that a cellular receptor known as GPR120 seemed to bind omega-3s and was present on immune cells involved in inflammation. When the team doused GPR120-containing mouse immune cells (pictured) with omega-3 fatty acids, that "shut down almost all of the inflammatory pathways," Olefsky says.

What's more, mice fed a high-fat diet became obese and developed diabetes (which has been linked to inflammation), but when the researchers added omega-3s to the diet, the mice experienced fewer diabetic symptoms. In fact, the supplemented diet worked as well to combat insulin resistance as the common diabetes drug Avandia. Mice lacking the GPR120 receptor remained diabetic regardless of how many omega-3s they consumed, the team reports in *Cell*. Still, Olefsky's not recommending that anyone take fish oil pills to stave off inflammation or diabetes until more research is done. http://bit.ly/fish-oil

Read the full postings, comments, and more at **news.sciencemag.org/sciencenow**.

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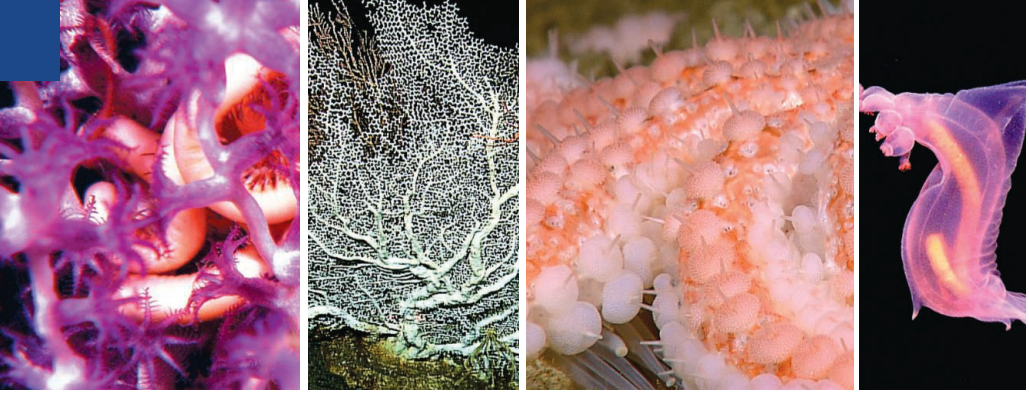


Secret Indonesian world. A brittle star, stony coral, 10-armed sea star, and swimming sea cucumber (*left to right*) were among the creatures sighted by a deep-sea rover.

BIODIVERSITY

Joint Expedition Discovers Deep-Sea Biodiversity, New Volcanoes

The shallow water reefs of the Coral Triangle, which stretches across Indonesia and north through the Philippines, host the world's greatest diversity of corals, fish, crustaceans, mollusks, and marine plant species. Now preliminary results from a joint Indonesian–U.S. marine survey indicate that the biodiversity runs deep. A remotely operated vehicle (ROV) has captured stunning images of massive corals, as well as unusual crustaceans and fish living at depths never before surveyed, thousands of meters below the surface. And mapping of that sea floor has turned up a huge, previously unknown volcano.

"I've done [marine surveys] for almost 20 years, all around the world, and I haven't seen things like this before," says Timothy Shank, an evolutionary biologist at Woods Hole Oceanographic Institution in Massachusetts. Indonesian and American researchers will be presenting preliminary results from the 24 June to 7 August two-ship expedition at the December meeting of the American Geophysical Union in San Francisco.

Stephen Hammond, chief scientist for ocean exploration at the U.S. National Oceanic and Atmospheric Administration (NOAA), says researchers have long wanted to explore the deeper waters of the Coral Triangle, but gaining permission for foreign research ships to enter territorial waters proved a stumbling block. The Obama Administration made research cooperation with developing countries a priority and found a willing partner in Indonesia (*Science*, 11 June, p. 1339). Subsequent discussions between scientists from the two countries led to a plan for joint, annual expeditions over the next 5 years by NOAA's *Okeanos Explorer*, a former naval surveillance ship converted for exploration in 2008, and Indonesia's *Baruna Jaya IV*, a marine survey vessel. The *Baruna Jaya IV* handles mapping and sampling down to 2000 meters, whereas the *Okeanos Explorer* probes more deeply: It uses a new sonar for mapping and *Little Hercules*, an ROV capable of diving to 4000 meters, for imaging.

For the first trip, the team visited sites in the Sulawesi and Molucca seas off Sulawesi Island. "We've had few opportunities to explore these waters," says Sugiarta Wirasantosa, an earth scientist at Indonesia's Agency for Marine and Fisheries Research.

The *Okeanos Explorer* and its ROV are equipped with state-of-the-art high-definition cameras and broadband communications links that allowed scientists at command centers in Jakarta and Seattle, and elsewhere, to view the sea-floor images and direct operations in real time. With this technology, "we have the opportunity to engage more scientists," Wirasantosa says. Shank says that at one point while in a hotel room in South Carolina, "I was leading the dive through my laptop, conversing through Skype, and getting a video feed from the sea floor."

One of the main objectives was mapping. It was known that geologic processes had produced "lots of ups and very deep downs," says Hammond. Beneath the Molucca Sea is a rare double subduction zone where tectonic plates encroaching from east and west are like a vise, squeezing a sliver of Earth's crust known as the Molucca Sea Plate. They are forcing the plate down into the mantle. A pair of nearly

BIODIVERSITY

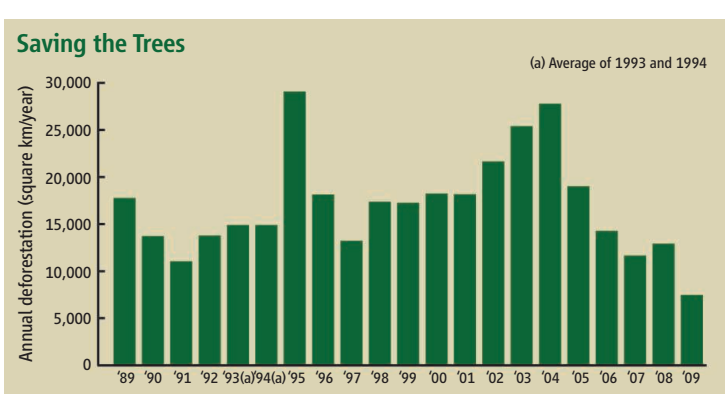
Brazil Says Rate of Deforestation in Amazon Continues to Plunge

SÃO PAULO, BRAZIL—Large-scale deforestation in the Amazon has declined by 47.5% over the past 12 months, according to a preliminary survey by the Brazilian Ministry of Environment using a low-resolution satellite. The figure is one of the largest declines since measurements began 20 years ago. If confirmed by a second set of satellite measurements due out later this year, it would mean more than an 80% drop in forest loss since a 2004 peak.

"I think the results are pretty strong for a big additional decrease in deforestation," says Greg Asner, a satellite expert with the Carnegie Institution for Science at Stanford University. "I am really pleased to see it. I do not doubt that the trend is real."

Brazil's remote-sensing agency, the Instituto Nacional de Pesquisas Espaciais (INPE), said last week that large fires burned half as much ground between August 2009 and July 2010 as during the preceding 12-month period. Clearing was concentrated in the agricultural states of Pará and Mato Grosso.

The release of the data has political overtones 1 month before the presidential election. Environment Minister Izabella Teixeira called the figures the "lowest of the low" and credited government enforcement



Green data. The amount of land being deforested annually has dropped sharply since a 2004 peak.

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parallel, active volcanic ridges run north to south near the colliding edges of the plates, where there are also many earthquakes.

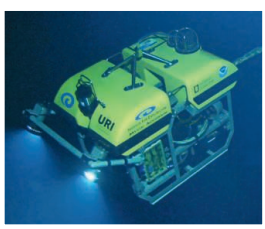
What the scientists saw was jaw-dropping. The new sonar on the *Okeanos Explorer* captured the topography in much greater detail than previous mapping efforts. One of the highlights was mapping in detail a little-known underwater active volcano along the west ridge. Rising 3800 meters from the sea floor, it's almost as tall as any of Indonesia's terrestrial volcanoes, yet its peak is still 1855 meters below the sea surface.

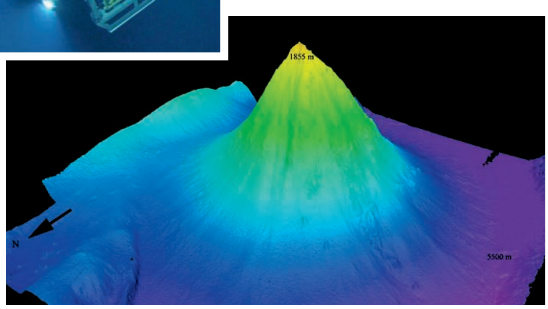
The tectonic activity also produces hydrothermal vents and other features that support marine life. Shank conservatively estimates that they saw 40 new deep-sea coral species. One "humongous" branching coral, a meter wide and a meter tall, "could be upwards of 6000 years old," he says. It is whitish because it does not host the colorful algae that give shallow-water corals their pastel hues. The corals and vents were home to an estimated 60 new species of shrimps, crabs, barnacles, and sea cucumbers, many of which probably evolved to exploit niche habitats. "For an evolutionary biologist, it's really cool," he adds.

Although the ROV cannot collect samples or measure temperatures, Shank says the high-resolution images capture anatomical details that make them confident they are looking at new species. But he concedes that they probably need samples and DNA analyses before they can add the new creatures to official lists.

Hammond says a new ROV able to measure temperatures and collect fauna, rock, and water samples could be available as early as next year. But it's doubtful the researchers will go back and try to capture the creatures they saw this year. Their objective is exploration rather than research, he says. So they are more likely to go in search of new volcanoes and new deep-sea denizens. The deep ocean "is hugely unexplored," he says. "Our mission is to try to make a dent in that."

"I can't wait to see the results" from a cruise "to the most exciting part of the ocean," says Meryl Williams, a former director general of The WorldFish Center in Penang, Malaysia, and a member of the Census of Marine Life steering committee. She also favors additional expeditions, noting that large swaths of the oceans "haven't been touched yet." **–DENNIS NORMILE**





Sea peak. A new sonar system and an ROV called Little Hercules (*inset*) led to the mapping of this underwater volcano.

CREDITS: COURTESY OF NOAA OKEANOS EXPLORER PROGRAM

efforts, including cutting off loans to those clearing large amounts of forest for cultivation. Greenpeace in Brazil, however, says the government's use of such preliminary figures is "propaganda." Adalberto Veríssimo, senior researcher at Imazon, a nonprofit in Belém that analyzes satellite data, says a further drop would be impressive, especially in an election year when enforcement is typically lax. "I was expecting the numbers to go up."

Researchers say the data come with several asterisks. The low-resolution system, known as the Real-time Deforestation Detection System, detects only fires covering more than 25 hectares. Indeed, Gilberto Câmara, general director of INPE, said that farmers may now be employing smaller conflagrations to escape detection, and the agency reported a large increase in the number of fires last month. He believes a more accurate survey known as Prodes, due out in November, will show a smaller decline. "We are seeing a process of consolidation in the Amazon, with no new frontiers, fewer large-scale cuts, and more small fires to expand existing farms," he says.

Daniel Nepstad, a senior scientist at the Woods Hole Research Center in Massachusetts, says that recent decisions by large food processors and supermarkets not to buy soybeans and beef from newly deforested areas has helped to slow the rate of deforestation. Some landholders may also be conserving forests in hope of receiving carbon credits.

But Nepstad worries that the picture could change for the worse if prices for agricultural products, depressed because of a sluggish economy, begin to rebound. "I think the bigger question is, 'When the prices come up, will Brazil's government be able to hold the line?' "

–ANTONIO REGALADO

Antonio Regalado is a writer in São Paulo, Brazil.

ScienceInsider

From the *Science* Policy Blog

Stanford University archaeologist Ian Hodder, who has directed excavations at Turkey's Çatalhöyük since 1993, has told the **heads of the dig's specialty labs that they will be asked to step down** beginning in 2012. One team member called it "the night of the long knives," but Hodder says that he's simply looking for "new energy" as he continues exploring the 9500-year-old site famed for its art and symbolism at the dawn of agriculture. http://bit.ly/catalhoyuk

A new report to President Barack Obama from his science advisers urges the federal government to **improve science and math education in U.S. schools** by both leading the way and rooting from the sidelines. The report backs more special science schools, a network of master teachers, and better use of technology in the schools. http://bit.ly/STEM-report

Catherine DeAngelis, the outspoken editor of the *Journal of the American Medical Association*, is stepping down after a 10-year tenure. DeAngelis, a pediatrician who was the first female editor of the journal, says that "all good things must come to an end." She'll be returning to Johns Hopkins University School of Medicine. http://bit.ly/JAMA-editor

The Obama Administration plans to **pare down the list of export-controlled items** and improve coordination between the different agencies responsible for granting export licenses. The academic community applauded news of the new list, which will be tiered by risk. A significant percentage of items are likely to be removed from lists altogether. http://bit.ly/export-controls

Two British software engineers have unveiled a project they hope will make **climate change science more transparent**. The project, called the Climate Code Foundation, offers a simplified version of software used by the Goddard Institute for Space Studies in New York City. The pair also hopes to expand a movement to make computer codes more user-friendly and open-sourced. http://bit.ly/climate-code

For more science policy news, visit **news.sciencemag.org/scienceinsider**.

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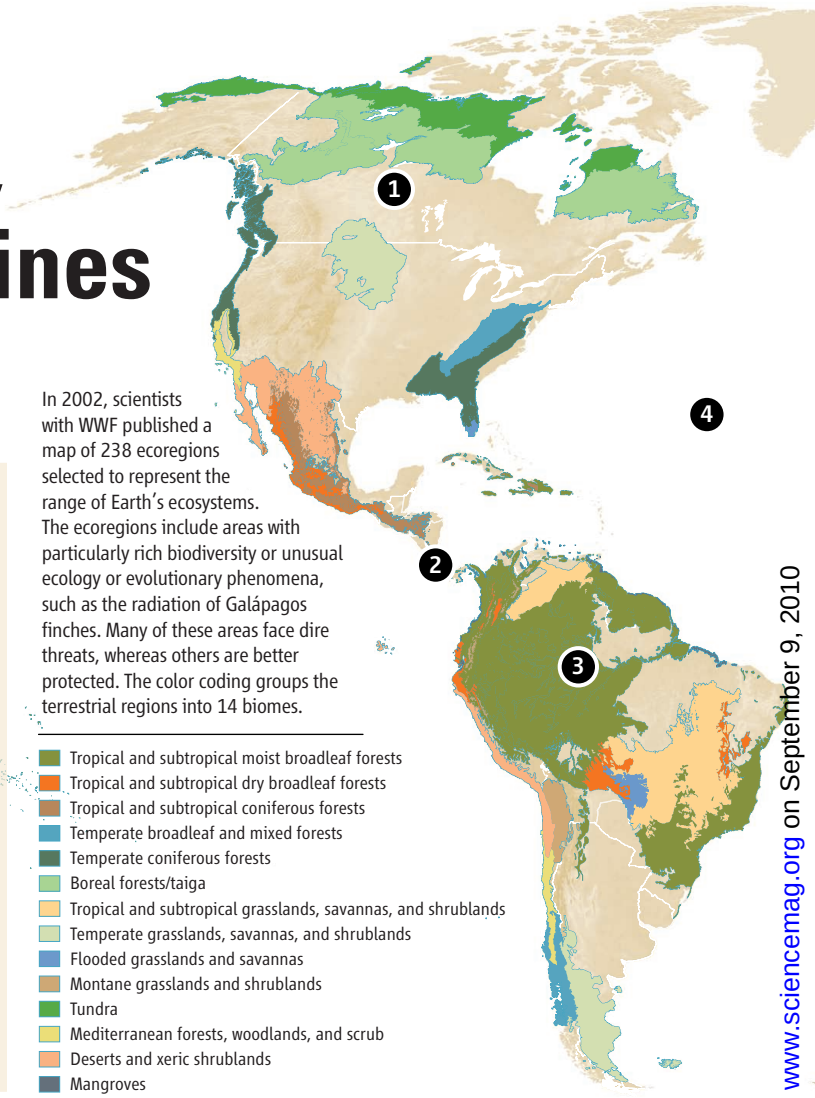
Despite Progress, Biodiversity Declines

After failing to meet its major conservation goal, the Convention on Biological Diversity is setting new targets for stemming the loss of species

2010, THE INTERNATIONAL YEAR OF BIODIVERSITY, CELEBRATES Earth's glorious variety of species and ecosystems. But many are threatened or damaged. This special News Focus section and a Review on page 1298 take a broad look at the global status of biodiversity and conservation.

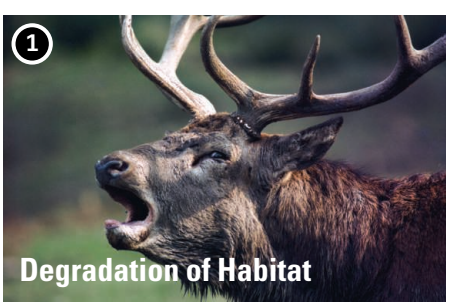
The principal international effort is a 1992 treaty called the Convention on Biological Diversity (CBD), which has failed to meet its lofty goal of a significant slowdown in biodiversity loss by 2010. Next month, CBD meets to adopt a new strategic plan.* The draft revises several of the 21 previous subtargets, such as controlling invasive species and creating more nature reserves. Below, we examine the major modifications proposed for six central targets, which will be negotiated 18 to 29 October in Nagoya, Japan. For each, we include a recent example of an advance or setback, as well as the assessment of progress by CBD's *Global Biodiversity Outlook 3*, published in May. The charts show the change over time of key parameters. These global trends mask large regional variation, some of which is explored in the following pages. **–ERIK STOKSTAD**

*www.cbd.int/doc/meetings/cop/cop-10/official/cop-10-09-en.pdf

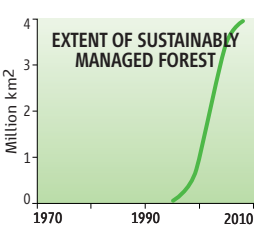


In 2002, scientists with WWF published a map of 238 ecoregions selected to represent the range of Earth's ecosystems. The ecoregions include areas with particularly rich biodiversity or unusual ecology or evolutionary phenomena, such as the radiation of Galápagos finches. Many of these areas face dire threats, whereas others are better protected. The color coding groups the terrestrial regions into 14 biomes.

- Tropical and subtropical moist broadleaf forests
- Tropical and subtropical dry broadleaf forests
- Tropical and subtropical coniferous forests
- Temperate broadleaf and mixed forests
- Temperate coniferous forests
- Boreal forests/taiga
- Tropical and subtropical grasslands, savannas, and shrublands
- Temperate grasslands, savannas, and shrublands
- Flooded grasslands and savannas
- Montane grasslands and shrublands
- Tundra
- Mediterranean forests, woodlands, and scrub
- Deserts and xeric shrublands
- Mangroves



2010 goal: Decrease the rate of loss and degradation of natural habitats.

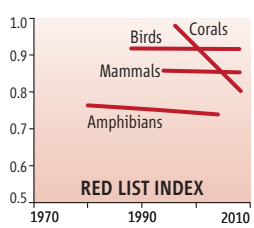


Progress: "Some." Many regions rich in biodiversity, such as Indonesia, continue to lose habitat. In the Amazon and a few other places, conservation action or economic recession has slowed the loss. Sustainable forestry is expanding but remains small.

Good news: In May, Canada's largest timber companies agreed to caribou protection and ecosystem-based management of 72 million hectares of boreal forest.

2020 goal: Halve or nearly eliminate the rate of loss, degradation, and fragmentation of habitat.

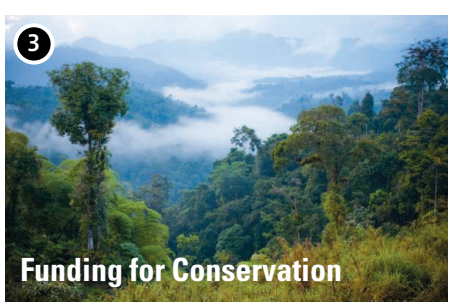
2010 goal: Restore, maintain, or reduce the decline of populations of species of selected taxonomic groups.



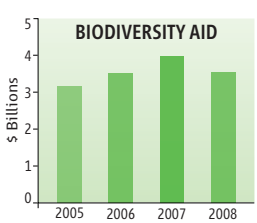
Progress: "Some." In some countries, conservation efforts have helped species recover. Yet overall, more and more are in trouble. (A value of 1.0 on IUCN's Red List Index means no extinctions are likely in the near future.)

Bad news: The golden toad (*Incilius periglenes*) of the cloud forests in Costa Rica was declared extinct in 2008. Global warming, pollution, and disease contributed.

2020 goal: Prevent the decline and extinction of known threatened species; improve the conservation status of at least 10% of these species.



2010 goal: To transfer new financial resources to developing country CBD participants.



Progress: "Some." From 2005 to 2007, official aid increased from about $3.1 billion to nearly $3.9 billion, but the emphasis is shifting to fighting climate change. Even rich countries spend just a tiny fraction of their national budgets on biodiversity.

Good news: New money being invested to prevent climate emissions from deforestation will help save biodiversity. In 2008, Norway contributed $1 billion to Brazil's Amazon Fund.

2020 goal: Increase 10-fold the human resources and financing for implementing the convention.

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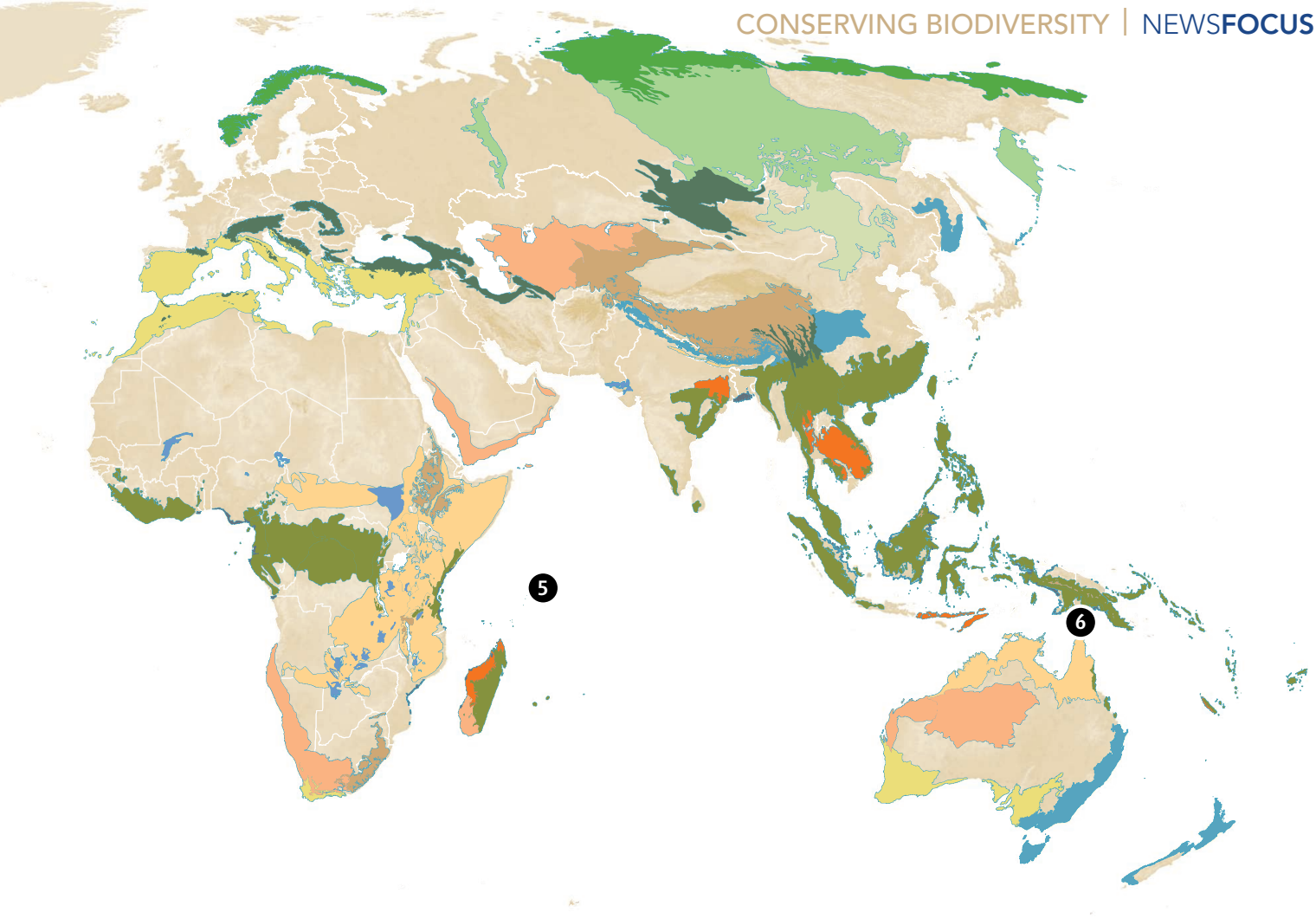
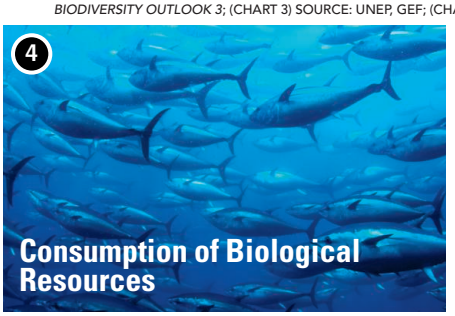
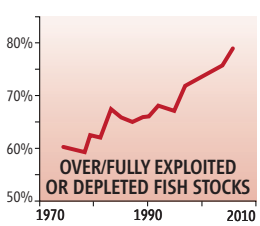


CREDITS: WWF'S GLOBAL 200 ECOREGIONS; D. OLSON AND E. DINERSTEIN, *ANN. MISSOURI BOT. GARD.* **89**, 199 (2002); (CHARTS 1, 2, 4, 5) ADAPTED FROM CONVENTION ON BIOLOGICAL DIVERSITY (2010) *GLOBAL BIODIVERSITY OUTLOOK 3*; (CHART 3) SOURCE: UNEP, GEF; (CHART 6) ADAPTED FROM S. BUTCHART *ET AL.*, *SCIENCE* **328**, 1164 (2010)



2010 goal: Reduce unsustainable consumption of biological resources or other consumption that harms biodiversity.

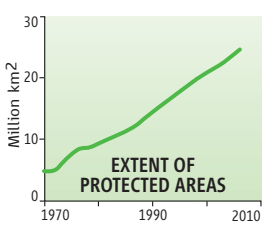


Progress: "None." The goal has not been met globally and is a major reason for biodiversity loss.

Bad news: Prized for sushi, the northern bluefin tuna is considered critically endangered. In March, conservation groups failed in their attempt to get an international ban on trade.

2020 goal: Continue to reduce consumption, with a new goal to end overfishing and destructive fishing practices, such as using dynamite or poison.

2010 goal: Effectively conserve at least 10% of each of the world's ecological regions.

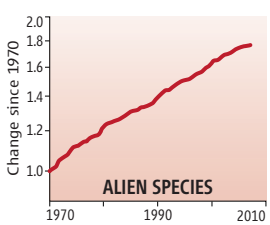


Progress: "Significant." The target has been achieved for more than half of the terrestrial ecoregions. Overall, 12% of all land is protected, but less than 0.5% of the oceans.

Good news: In May, the United Kingdom designated the Chagos Archipelago as the largest marine reserve in the world, setting aside 544,000 square kilometers.

2020 goal: Protect 15% to 20% of land. CBD has not proposed a figure for coastal and marine ecosystems. The draft target emphasizes that protected areas should be interconnected and well-managed.

2010 goals: Establish management plans and control the pathways for major potential invasive species.



Progress: "Some." Global trade and travel continue to spread alien species, some of which become invasive. Most countries don't have management plans.

Bad news: The voracious snakehead fish (*Channa striata*) of tropical Asia has spread around the world. Around 2007, it arrived in southern Papua New Guinea and is eating native fishes.

2020 goal: Prioritize control efforts. The target outlines the steps to be taken.

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Tending the Global Garden

By sorting out plant names and growing threatened species, botanic gardens try to do their part for plant conservation

In 2008, Gustavo Martinelli was worried. Six years earlier, his country, Brazil, had signed onto an international plant conservation initiative, and the first order of business was to develop a comprehensive list of the nation's plants by 2010. The last such list of Brazil's flora, completed in 1906, took 60 years to put together. But less than 2 years from the deadline, work on the new tally hadn't even started, recalls Martinelli, a taxonomist at the Rio de Janeiro Botanical Garden. And if this initial task fell behind schedule, it would push back other key goals of the conservation initiative, such as figuring out which plants were threatened and safeguarding a certain percentage of those at risk. "There will never be a good endangered species list if we can't have a list of the flora," Martinelli says.

So Martinelli and botanical garden colleague Rafaela Forzza rallied 413 taxonomists from Brazil and elsewhere for what seemed at first like an impossible push. In a matter of months, they were to check through the names gathered from regional plant lists, picking out the correct names for each species and sorting out all synonyms, to come up with a master record. The due date was the end of 2009, and over the Christmas holiday, the Web site where people were submitting their responses was abuzz with activity. "It was very amazing to see everyone trying to do their part," says Martinelli.

Thanks to that effort, Brazil is now one of the few countries that can boast of having an online database where researchers, conservationists, and the public can examine the distribution and other information about each plant, some 41,000 species. Brazil's taxonomists aren't the only ones who have been hustling. As part of the same initiative—the Global Strategy for Plant Conservation—that motivated Martinelli, botanists and computer experts from the Royal Botanic Gardens, Kew, in the United Kingdom and the Missouri Botanical Garden in St. Louis are striving to finalize a list of the known plant species in the world before the year's end.

The rush is because 2010 looms large as the deadline for this and many other goals set forth in the Convention on Biological Diversity (CBD), an international treaty on the conservation of flora and fauna worldwide (*Science*, 14 January 2005, p. 212). Conservationists are now taking stock of their successes and failures at protecting biodiversity as the convention promised (see p. 1272). In addition to leading efforts to tally the world's plants, botanic gardens have made progress in setting up seed banks and native plant collections. In some cases, they have even reintroduced endangered species back into native habitats.

For some plant aficionados, however, too little has been accomplished. Botanic gardens and other organizations have struggled to identify which plants are threatened. Moreover, despite some progress, the gardens are far from achieving the collections and restoration goals incorporated into CBD. "It doesn't look like we've made significant progress," says W. John Kress, a botanist at the Smithsonian National Museum of Natural History, who worries that the ongoing destruction of plant habitats, compounded by climate change, dwarfs any plant conservation advances made by having these targets.

But others say the very process of establishing goals has had an impact. "Without those targets, an awful lot less plant conservation would have been achieved," asserts Peter Wyse Jackson, who just became president of the Missouri Botanical Garden.

CREDIT: OMAN BOTANIC GARDEN

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Planting seeds. At the Oman Botanic Garden, students learn how plants keep nature in balance.

CREDIT: RBG KEW

A new purpose for botanic gardens

Plant conservation hasn't always been part of the mission of botanic gardens. They got their start in the 16th and 17th centuries as homes to medicinal plants and later as places to cultivate newly discovered species brought back from worldwide explorations. Until recently, the key scientific activity for many botanic gardens was merely collecting and labeling seeds and plants. The idea that such gardens should look beyond their walls and fences to help preserve plants in their native habitats emerged slowly. "Traditionally, many botanic gardens have been somewhat resistant to [having] conservation as a main activity," says Peter Raven, retired president of the Missouri Botanical Garden.

That has now changed. Botanic gardens have come to play a pivotal role in standing up for plants, in part because few other organizations were willing to devote time and money to plant protection. "There's been a fundamental shift in botanic garden policies over the last 2 decades," says Wyse Jackson. Many, though not all, gardens now place a much greater emphasis on conservation, plant genetics, and educating the public about the importance of preserving plant biodiversity. More gardens are also adding collections of native plants to complement their exotic species.

A turning point came in 1999, at the International Botanical Congress in St. Louis. There, Raven appealed to the broader botanical community and was cheered when he called for a global initiative to save plants. By 2002, botanists, policymakers, and other interested parties had come up with the Global Strategy for Plant Conservation: 16 specific targets or goals ranging from a worldwide list of plants to conserving plants and educating the public. That same year, national delegates approved incorporating the strategy as part of CBD.

Online
sciencemag.org
Podcast interview with author Elizabeth Pennisi.

This conservation initiative "brought everyone into a common framework" around which efforts could be organized, says Sara Oldfield, secretary general for Botanic Gardens Conservation International (BGCI), an umbrella organization of the gardens, based in Richmond, United Kingdom. And for the first time, CBD had concrete goals—with a 2010 deadline.

Reaching those goals, in the time allotted, would be a tall order, everyone realized. "We knew they were all very challenging targets that went well beyond what could be achieved by business as usual," says Wyse Jackson. Botanic gardens were not in a position to work on all the targets; they had no control over whether agricultural lands were managed sustainably, for example. But they saw themselves as key players in developing a list of all known plants, assessing the conservation status of plants, establishing so-called ex situ collections and recovery programs, and education.

Making lists

The first order of business, coming up with a catalog of the world's plants, is harder than it sounds. The same plant may wind up with multiple genus and species names as people in different places, or at different times, describe it without realizing they're documenting something already named. As a result, there are about a million names on record for an estimated 370,000 or so plants.

Sorting out these synonyms is tedious work, and not glamorous enough to attract much funding. But without knowing all of a particular plant's synonyms, conservationists would be unable to determine the full range of a species or whether it is truly rare. And that leads to poor conservation planning, says Kew bioinformatician Robert Allkin. For example, a Kew conservation project has taken a close look at the plants named on Botswana's official Red List of Threatened Species. It found that 40% of the names had problems, ranging from spelling errors to a plant that looked to be endangered but, when all its synonyms were taken into consideration, was really quite common in the African country.

Over the decades, Kew taxonomists had been going through their records and the botanical literature, plant family by plant family, trying to come up with a master list of plants with their synonyms sorted out. But it was slow going, and little additional funding turned up to do the work. By 2007, "it was obvious that going at the pace we were going, we wouldn't get there," recalls Kew taxonomist and public policy expert Eimear Nic Lughadha.

Then Chuck Miller, a bioinformatics expert at the Missouri Botanical Garden, had an idea: Let computers figure out the conflicting names. The taxonomists "started off thinking there was no way you could do this," he recalls. But Miller gradually convinced them that a computer-generated list of plants, while imperfect, would provide a "good enough" starting point for conservationists, one that could be improved upon over time by in-person evaluations.

The plan was to pool and compare existing digitized plant lists, including a world checklist that Kew had been pulling together, and Tropicos, a database started at the Missouri Botanical Garden in 1982. The researchers also made use of the International Plant Names Index, which for more than a century has collected all plant names.

These various lists contain multiple names for many species, each designating a main name and synonyms. When the project's computer program spots inconsistencies between the lists as to which name is the primary one versus a synonym, it uses predetermined rules to decide which one is correct. For example, the program considers more recent information better than older data, because newer publications likely took into account the older literature. It also favors names that

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Global coverage. The Oman Botanic Garden, Xishuangbanna Tropical Botanical Garden in Yunnan Province, China, and Royal Botanic Garden in Jordan (*top to bottom*) are just a few of some 2600 botanic gardens, many of which have conservation as a goal.

have wider geographic distributions or that come from a monograph, the traditional way botanists introduce a new species, as opposed to another type of article.

Before Miller and his colleagues fired up their software, taxonomists had taken years to show that some 267,000 plant names represented just 174,500 species. But there were still roughly 450,000 names left to evaluate.

In June, at the Fourth Global Botanic Gardens Congress in Dublin, Miller and Allkin unveiled a new version of the world plant list that had been aided by computational name resolution. The software had settled on 255,000 plant names, designating 430,500 others as synonyms. There were 95,977 additional names still unresolved because adequate data were lacking. The hardest plants to sort out were those from Southeast Asia, where few computerized lists exist, says Nic Lughadha. The analysis presented in Dublin hadn't yet included databases for the legumes; composites, the group that includes daisies; and grasses. These contain 264,000 names but only an estimated 59,000 species and will be incorporated and resolved by October.

While Miller and colleagues acknowledge that the global list of plant names won't be perfect by the end of the year, they believe it will be good enough to help achieve other conservation goals. One such goal, the second target of the Global Strategy for Plant Conservation, is to assess how endangered each known plant is.

Meeting that goal has been even more of a struggle than compiling the list of names. Although the global strategy doesn't specify how the conservation status of a plant should be determined, the criteria by which the International Union for Conservation of Nature (IUCN) determines its "Red List" of threatened species has become the de facto standard. Yet although IUCN's Red Lists have been around since the 1980s, they traditionally focused on animals. Not until 1997 did a major compilation of threatened plants appear. It concluded that 34,000 of the 75,000 evaluated were under some sort of threat.

Even as botanists were laboring away on the 1997 plant Red List, however, IUCN was changing its criteria, standardizing how potential listees were evaluated. So the 1997 plant effort was outdated before it was even completed. A mere 12,189 plants have been assessed to date using the new IUCN criteria, and of those, about 9000 were judged to be in trouble to some degree. "It takes quite a lot of experience and time to gather that data," says BGCI's Suzanne Sharrock.

It also takes money, and no global organization, environmental group, or other funder has committed resources to a worldwide assessment of individual plant species. "Plant conservation is just not a popular cause," says Oldfield. "It has failed to capture the popular and political imagination."

There has been progress with other types of conservation assessments. Kew, for example, has developed a computer program that enables its taxonomists to sift through their data on a species and readily determine the range, distribution, and other conservation parameters of a species as a first pass on its conservation status. Individual countries are tackling the issue as well, many of them using their own criteria to create national plant Red Lists: South Africa, for example, just finished assessing its 20,000 plant species, concluding that 5000 are threatened.

Still, a global Red List of threatened plants won't be available by 2010. "We haven't done very well," acknowledges IUCN's Craig Hilton-Taylor.

Digging in for conservation

Botanic gardens and other institutions have been working hard to save those plants already identified as in jeopardy. For 2010, the global strategy called for 60% of threatened plants to be conserved outside their natural habitats. These ex situ collections could comprise live plants, seed banks, or even tissue collections. In addition, by this year, 10% of threatened species were supposed to have programs promoting their recovery and restoration. There's been modest progress toward both goals. In 2002, just an estimated 15% of threatened plant species had been incorporated into in these ex situ

CREDITS (TOP TO BOTTOM): OMAN BOTANIC GARDEN; PETER WYSE JACKSON (2)

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Back from the brink. After conservationists discovered a supposedly extinct fern, *Anogramma ascensionis* (*right*), they collected spores for cultivation in a botanic garden before reintroduction into the wild.

CREDITS: ASCENSION ISLAND GOVERMENT CONSERVATION DEPARTMENT

collections, with only 2% in recovery projects. By 2007, the numbers were 35% and 5%, respectively, according to the Convention on Biological Diversity Plant Conservation Report assessing progress on the initiative. But Wyse Jackson points out that the lack of a global Red List for plants makes it difficult to know how accurate these numbers are.

No new figures on either of these goals were released at the Dublin meeting, but Kew continues to spearhead the Millennium Seed Bank project, a 50-country effort that has already gathered and stored seeds from 24,000 species—an estimated 10% of the wild species—and aims to cover 25% by 2020. New botanic gardens in Oman and Jordan are also specializing in collecting arid land plants from their respective regions. And places such as the National Botanic Gardens of Ireland and the Royal Botanic Garden Edinburgh have expanded efforts to cultivate and restore the native flora within their country's borders.

A similar push is ongoing in China, where some 160 botanic gardens exist, about a dozen of which are organized into a network run by the Chinese Academy of Sciences. China has an estimated 33,000 native plant species, some 19,000 of which are currently growing in its botanic gardens. And in the next 5 years, says Huang Hongwen of the South China Botanical Garden in Guangzhou, that number should increase to almost 25,000, with many species represented in multiple places as an added precaution. One garden alone, the Xishuangbanna Tropical Botanical Garden, rapidly expanded its ex situ collections, from 4000 species in 2002 to 10,000 in 2005.

For China, progress on conserving species and meeting the ex situ conservation target is mired in red tape. On the one hand, all 388 plant species on the Chinese government's 1992 Red List—the last time one was compiled—are now growing in botanic gardens. But, says Huang, 4404 species are now being considered for red-listing. The government's delay in approving this new Red List has slowed decisions on spending money to place some species in ex situ collections. "It's a problem," says Huang.

Still, the South China Botanical Garden is pushing ahead with some recovery and restoration efforts. The garden set up the country's first nature reserve in 1959 and now uses its experience to help guide many of the more than 3000 in China today. There are now more than 40 plant species in recovery programs across the country. One medicinal plant, *Myricaria laxiflora*, lost its entire habitat with the building of the Three Gorges Dam. It was kept alive in gardens for more than a decade and has recently been replanted in a new habitat, says Huang.

Many other botanical gardens have select plants that they have worked hard to save from extinction and now plan on reintroducing. The Tooro Botanic Garden in Uganda has been cultivating 94 tree species, many of them rare and endangered, and now has 40,000 saplings from those species almost ready to be transplanted into natural habitat. Kew is nurturing a fern to reintroduce onto Ascension Island; it was thought to be extinct, but a few specimens were recently found and spores were sent to Kew for cultivation.

Yet finding an appropriate home for plants may become tougher as climate change and pollution—two factors barely considered when the CBD plant goals were set in 2002—increasingly alter the world. In Ireland, "our best estimate is that at least 20% of the native flora will likely become extinct due to climate change this century," says Wyse Jackson.

That the native habitats of many plants are becoming unsuitable homes has made ex situ collection a higher priority, say conservation scientists. They are therefore updating their global plant conservation strategy and have proposed a 2020 goal of having 75%, instead of 60%, of endangered plants in protective programs, and 20%, not 10%, targeted for recovery and restoration, says Wyse Jackson.

Like the plants they're trying to save, botanic gardens face a myriad of threats themselves. In the developing world, where botanic gardens struggle to get any funding, "many governments are beginning to focus in on one priority, poverty," says Stella Simiyu of BGCI. She argues that to stay relevant and survive, botanic gardens in such places will need to focus on facilitating the sustainable use of plants, particularly of medicinal plants, which are in high demand and have dwindling numbers. They will need to partner with government and nongovernmental agencies to coordinate education programs that help promote judicious use or protection of rare resources. "Typically, botanic gardens don't work like that," says Simiyu.

For all botanic gardens, funding will continue to be an issue. To date, "what has been achieved has been primarily through internal reprioritization," says Stephen Blackmore, Regius Keeper of the Royal Botanic Garden Edinburgh. But, notes Wyse Jackson, "if we are to achieve the targets for 2020, then new resources must be found."

Yet at many botanic gardens, funding may get tighter as countries struggle to lift themselves out of the worldwide recession. Kew, for example, is apprehensively waiting to hear how it will fare in the new British government's austerity push. Nic Lughadha worries that funding woes and the resulting reduced travel by botanic gardens staff members could lead to a conservation retreat, wherein researchers simply mind existing collections and cease to reach out to communities that were the sources of the plants. That would be a big mistake, says Blackmore, because "we must scale up in situ conservation," he explains. "We're doing it, but we are not doing it on a big enough scale. Biodiversity is losing out despite our best efforts."

–ELIZABETH PENNISI

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Saving Forests To Save Biodiversity

A hot spot for undiscovered flora and fauna, Indonesia begins to take steps to preserve its forests and its biological heritage

On guard. Patrols to thwart illegal logging support efforts to restore an ecologically precious forest.

CREDIT: CLARE KENDALL/RSPB

In a dozen or so field trips to Borneo over the past 5 or 6 years, Daisy Wowor rarely went home without a new species. A freshwater crustacean specialist, she has described eight already, and a 2-week field trip earlier this summer has likely netted two new crabs and, possibly, a new prawn. Finding undiscovered nuggets of biodiversity "is quite exciting, I can tell you," says Wowor, a staff scientist at the Indonesian Institute of Sciences in Bogor.

Wowor is not the only one experiencing that excitement. Over the past decade, scientists on Borneo have found insects, plants, fish, and even a bird that are new to science at the rate of about three per month. Heok Hui Tan, a freshwater fish expert at the National University of Singapore, has identified more than two dozen new species. "And we have another 40 or 50 specimens that could be new species awaiting study," Tan says.

This hidden diversity is not just on Borneo. On New Guinea, which Indonesia shares with Papua New Guinea, recent expeditions to the remote Foja Mountains on the island's northern edge have also produced bumper crops of novel organisms. "We have not explored our country properly, so the chance to [find] new species is quite big," Wowor says.

Yet even as scientists are documenting Indonesia's biodiversity (see also p. 1270), it is increasingly threatened. The list of endangered plants and animals is long. And Indonesia may have the world's highest rate of deforestation. Wowor recalls pulling a couple of new crustaceans from a bend in a river in Borneo's East Kalimantan province in 2008. She went back to the site a year later and found that trees were being chopped down and that the bend in the river was dry, cut off by a stream-straightening project that also left the formerly clear water muddied and acidic. Given the pace of environmental destruction, "I have to work fast," she notes.

But she may be able to slow down a little. In the past 5 years, Indonesia has reduced illegal logging. There are new initiatives to restore degraded areas and protect the remaining forests, particularly a whopping $1 billion deal with Norway earlier this year to set aside large amounts of forest. And there is a new attitude among the public and Indonesia's political leaders. "The importance of these natural forests is being recognized more than before," says Agus Utomo, executive director of the conservation organization Burung Indonesia.

These developments are winning plaudits from conservationists, but although "there is progress, we cannot say it is sufficient," Utomo cautions. Meeting last month on Indonesia's Bali island, the Association for Tropical Biology and Conservation (ATBC) commended Indonesian President Susilo Bambang Yudhoyono for his conservation efforts but also urged him to do more to protect forests. The resolution's praise and constructive criticism "are both important to encourage attention and action from the national government," says Mochamad Indrawan, a conservation biologist at the University of Indonesia in Depok, who chairs ATBC's Asia-Pacific chapter.

Biodiversity hot spot

Indonesia's 17,000 islands straddle the equator and stretch over three time zones. The western islands were once connected to the Asian mainland; the eastern, to Australia, giving the country a double dose of flora and fauna. Indonesia contains 10% of the world's flowering plants, 12% of the world's mammals, and 17% of the world's reptiles, amphibians, and birds. And it hosts the largest populations of some of the signature species of Southeast Asia—the Javan and Sumatran rhinoceros, the Asian pygmy elephant, the Sumatran tiger, and several species of orangutan. Alfred Russel Wallace's studies of specimens collected in Indonesia and elsewhere in Southeast Asia led him to describe concepts such as survival of the fittest and natural selection in an 1858 paper presented even while Charles Darwin was writing *On the Origin of Species*.

Among these biodiversity treasure islands are two particular gems: the world's second-largest island, New Guinea, and the third-largest island, Borneo, shared among Brunei Darussalam, Indonesia, and Malaysia. On both islands, rugged terrain historically limited human settlement. The population of Borneo is still just 20 million and New Guinea, 7.5 million. Both populations are concentrated on the coastal fringes and along rivers. Neither island has experienced the human population pressures and agricultural development seen on Java, peninsular Malaysia, or through much of the Philippines. As a

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Fruitful fieldwork. Biologist Daisy Wowor finds new crustaceans every time she surveys Borneo's rivers.

result, both are still reservoirs of as-yet-to-be-discovered biodiversity.

Borneo is considered to be in a class of its own. It has coastal mangroves, lowland rainforest, and mountains ranging up to the 4095-meter Mount Kinabalu. And over geologic time, Borneo remained along the equator while tectonics moved other islands north and south.

Geological processes and Borneo's varied terrain combined to make the island a hothouse of evolution. Borneo has 15,000 species of flowering plants, a diversity three times that of neighboring Java. And 34% of those flowering plants are found nowhere else. It also has 155 tree species, 44 mammal species, and 37 bird species that are endemic. And more are being discovered every year.

But Indonesia has been a poor steward of its biodiversity. By the end of the 1990s, logging and clearing land for agriculture had decimated the forests of Java and Sumatra, and the destruction was spreading to Borneo. Through the 1990s, forest fires, most started intentionally despite laws against the practice, spread a haze of smoke over much of Southeast Asia. The fires that raged in 1997 and 1998 alone burned 6.5 million hectares, primarily on Sumatra and Borneo, and probably killed hundreds if not thousands of orangutans. Logging has endangered prized timber species, and habitat loss and illegal wildlife trading are threatening an increasing number of fauna. The International Union for Conservation of Nature found that Indonesia ranks fourth globally in the total number of species on its 2008 Red List of Threatened Species. Thus, while Indonesia can boast of the greatest number of mammal species, 670, in the world, it also has the most, 183, that are threatened. And Indonesia was second to Brazil in the number of birds on the Red List: 115, of which 67 are found only in Indonesia.

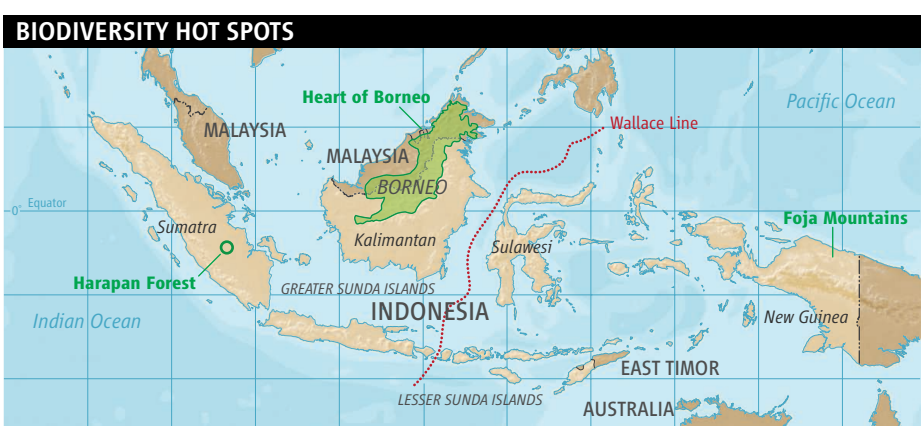
Saving forests

Through the 1980s and '90s, Indonesia's poor environmental record was blamed on the lack of interest and cronyism of the Administration of President Suharto, who ruled the country for 32 years. But after he resigned in 1998 and the country took its first steps toward democracy, the situation initially took a turn for the worse. Political power, long centralized in Jakarta, was dispersed to local authorities. Rogue timber companies took advantage of the chaotic transition by logging without permits, even taking trees in national parks. In 2004, Susilo Bambang Yudhoyono was elected president, partly on a platform of combating corruption. Shortly after taking office, he ordered the national police to lead a coordinated crackdown on illegal loggers and corrupt officials. The result has been a 75% reduction in illegal logging in Indonesia since 2000, according to Chatham House, a London-based think tank. The bad news is that the report estimates that 40% to 61% of the total timber harvest in Indonesia is still outside the law.

Sam Lawson, who has monitored logging in Indonesia since the 1990s and was the lead author of the study, says the Yudhoyono Administration targeted the most blatant transgressors: gangs logging without permits or obviously outside designated lumbering areas, called concessions. He says that in response to tightened enforcement, "they're a bit more cunning, illegally obtaining licenses" through bribery or falsified applications. What's needed are good timber-tracking systems and proper procedures for allocating harvest rights, Lawson adds.

Indonesia's turn to democracy has also made room for nongovernmental environmental organizations to be more influential. Working with the Ministry of Forestry, Burung Indonesia, founded in 2002, has helped establish a national ecosystem-restoration plan, which should be complementary to the national parks system. With international partners and support, Burung is restoring 98,000 hectares of a heavily logged area in central Sumatra known as the Harapan Rainforest. It also intends to promote sustainable use—though not commercial logging—by local communities.

Saving logged forests recently received a scientific endorsement in a paper published online on 4 August in the *Proceedings of the Royal Society B*. David Edwards, a biologist at the University of Leeds in the U.K., and colleagues compared species diversity in pristine, once-logged, and twice-logged forests in Malaysian Borneo. They focused on birds and dung beetles as indicators of broader biodiversity. Not surprisingly, the authors found that 30% of bird species and half of the dung beetle species either disappeared or were significantly reduced in number after one round of logging. The second round had little fur-



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Conservation and discovery. Indonesia is trying different approaches to protect and preserve natural habitat in the Heart of Borneo, Harapan Rainforest, and Foja Mountains.

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On the brink. Indonesia's endangered species include (*clockwise from top right*) the Sumatran tiger, Sumatran orangutan, Bawean deer, *Nepenthes aristolochioides* (a pitcher plant), Celebes crested macaque, and Western Long-beaked Echidna (*center*).

ther effect. Ultimately, however, more than 75% of the bird and dung beetle species found in the pristine area took up residence in the twice-logged forest, including a large number of threatened birds. The authors say their findings indicate that Indonesia and Malaysia should rethink current policies that favor turning degraded forests into oil palm plantations, which harbor just a fifth of the bird species found in primary forest and few if any species of conservation concern. "Preventing these degraded forests from being converted to oil palm should be a priority of policy-makers and conservationists," the authors wrote.

Burung, employing local villagers, has begun planting 5 million trees, starting in the most degraded areas. They are also guarding against illegal logging. Utomo says there is now evidence that a family of critically endangered Sumatran tigers with three cubs is in the area. "It's a good sign that the forest can be viable for big mammals," he says.

The efforts of another conservation organization, WWF, have also borne fruit. In the early 2000s, WWF became alarmed by the rapid loss of Borneo's forests. Studies indicated logging, fires, and clearing for plantations had cut forest cover from 74% of the island's total area in 1985 to 50% in 2005. The largest remaining contiguous tract of forest stretched over the borders of the three countries that share Borneo, and only about half of it was protected. Working at the level of national parks "was really missing something in terms of larger scale biodiversity conservation," recalls Adam Tomasek, WWF team leader for conserving this large tract.

WWF proposed the establishment of the transnational Heart of Borneo conservation area, an idea that found receptive ears. "The highlands of Borneo [hold] the last remaining intact forest, and it needs to be preserved," says Samedi, deputy director for protected area management in Indonesia's Ministry of Forestry, who like many Indonesians uses one name. Loosely following the example of the 10-country Congo Basin Forest Partnership, in 2007 the three nations jointly agreed to conserve and manage a 220,000-square-kilometer area sprawling over the center of the island (*Science*, 13 July 2007, p. 192).

About half of the Heart of Borneo was already protected. Indonesia is now drawing up special land-use regulations and guidelines that will require production forests, plantations, mines, and other commercial interests in the region to adopt sustainable management practices.

A third conservation initiative grew out of President Yudhoyono's promise to reduce Indonesia's carbon dioxide emissions by 26%. In 2009, he pledged to invest in renewable energy and to curb deforestation and land conversion, which account for 80% of the country's greenhouse gas emissions. But Yudhoyono went further, saying Indonesia would up the ante on emission reduction to 41% if there were international support.

Earlier this year, Norway accepted that challenge with a proposal that could pay Indonesia $1 billion over the next 7 to 8 years for verified emissions reductions through forest preservation. Under the 26 May agreement between the two governments, starting next January, Indonesia will issue no new logging permits for 2 years. By 2013, the country should have a strategic plan to reduce deforestation, one that has been tested in one or more pilot projects; an agency to execute it; and an institution to monitor and verify progress. In return Norway, and possibly other donors, will put some money on the table early to help start the process, but the bulk of the contribution will be delivered only when Indonesia succeeds in reducing deforestation-related emissions, and the sum will depend on how well it succeeds. The agreement runs through 2016 but could be extended.

Conservationists are generally impressed with this plan but want to see the details worked out and executed. "There is a potential for significant improvements" in managing the country's forests, says William Laurance, a tropical ecologist at James Cook University in Cairns, Australia. Nonetheless, "deforestation could continue for a long time, just under existing concessions," he adds.

Still, Laurance says it took "a certain level of courage" on the part of Yudhoyono to enter into the agreement with Norway. "The fact that the president was willing to enter into this very ambitious international agreement and to acknowledge the extent of the illegal logging is huge," Laurance says. But given the daunting challenges, it is risky. "There could be significant benefits from success but also significant [consequences] of failure both for Indonesia and for international efforts to conserve forests," he says.

One consequence of failure would be fewer opportunities for Wowor and her colleagues to experience the excitement of finding new species. **–DENNIS NORMILE**

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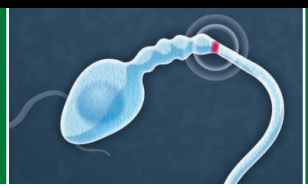

LETTERS

edited by Jennifer Sills

No Return from Biodiversity Loss

IN THEIR LETTER "BRAZILIAN LAW: FULL SPEED IN REVERSE?" (16 JULY, P. 276), J. P. METZGER and coauthors highlight the precarious plight of the Brazilian Forest Act (Código Florestal), embattled by new legislative reform that will effectively condemn old-growth remnants and forest regrowth in private landholdings throughout the largest tropical country on Earth. We would like to emphasize that the reforms could lead to irreversible loss of tropical biodiversity.

Rural private properties account for 39% of Brazil's ~8.5M-km^2 territory and represent an essential component of forest biodiversity conservation that is separate from formally protected areas. Sadly, the short-term interests of powerful economic groups, influential landowners, and politicians ignore the conservation value of private-sector forests by diluting the Brazilian Forest Act.

The detrimental environmental and social impacts of brushing aside scientific evidence are exemplified by the proposed reductions in protected forest area requirements for riparian forest (buffer strips) located adjacent to rivers and streams. Current proposals ignore pervasive edge effects, whereby the influences of neighboring habitats such as cattle pasture permeate into forest areas, gradually decimating the canopy tree population (*1*). The reduction in buffer strips means that these landscape features will have decreased ability to both retain and connect forest species (*2*) and maintain water quality and flows (*3*). Landowners who comply with the new legislation would increase landscape fragmentation and reduce the value of their properties as a result of property-scale soil erosion and poor water catchment regulation within watersheds (*4*).

Brazilian biodiversity at risk. Proposed legal reforms could cause irreversible loss of biodiversity and reduce the value of private properties.

There is a glimmer of hope: The scientific community, environmental nongovernmental organizations, and the Ministry of Environment can still reconcile with the staunch proponents of Brazilian Forest Act reform. We need better communication among all segments of society to develop wise land-use management of the existing agro-pastoral matrix, thereby sparing the need for further expansion of new deforestation frontiers.

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Overuse Could Leave Southwest High and Dry

IN THEIR PERSPECTIVE "DRY TIMES AHEAD" (25 June, p. 1642), J. Overpeck and B. Udall highlight serious water availability issues the western region of the United States may soon face in the form of less precipitation, longer drought patterns, and decreased snow pack. There is another risk as well: overapportionment.

In the Colorado River Basin, the water lifeline of southwestern United States, long-term planned use of the river's water exceeds the reliably available supply. Use agreements for the water in the Colorado and Rio Grande River basin are governed by laws and compacts between the southwestern states. Most of these agreements are 50 to 100 years old and were drafted on the basis of then-current water resource data, without taking demographic and climatic trends into account (*1*). Climate change is projected to increase the likelihood of a shortage (*2*). This situation could be worsened by the fact that the states in or adjacent to this corridor include some of the states with the highest population growth rates. The U.S. Census Bureau has projected

Letters to the Editor

Letters (~300 words) discuss material published in *Science* in the previous 3 months or issues of general interest. They can be submitted through the Web (www.submit2science.org) or by regular mail (1200 New York Ave., NW, Washington, DC 20005, USA). Letters are not acknowledged upon receipt, nor are authors generally consulted before publication. Whether published in full or in part, letters are subject to editing for clarity and space.

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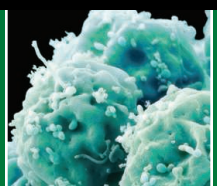
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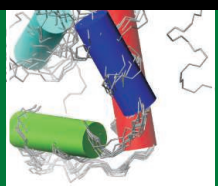
An exciting shift
1295

that an additional 10 to 13 million people will reside in these regions by 2030 (*3*). To add another layer of complexity, the possibility of basing an integrated industrial ecology on biofuels (such as algae and lignocellulose) has received increased attention in southwestern United States (*4*). However, the water footprint represents a major sustainability challenge for future biofuel production (*5*–*7*). In the future, increased demand for water for civic, agricultural, and even energy needs coupled with a decreasing supply could result in conflicts between states regarding water sharing, management, and use.

To address these issues and facilitate sustainable production of clean energy, state and federal governments should implement strict guidelines and a regulatory framework for water-use permits and water recycling. Commercial biofuel production permits should be given to companies and units that have implemented modern technologies for water recycling and conservation. New policies and regulations for water management and use should be a high priority for the sustainable development of a biofuel sector in order to meet liquid fuel needs in the United States without hampering the regional hydrologic pattern in the southwestern region of the country.

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Test Ban Results Could Be Negative

P. S. CORDEN'S HOPE THAT BANNING NUCLEAR tests will somehow bring nuclear peace ("Banning Nuclear Tests," Editorial, 21 May, p. 953) ignores much history. He neglects to acknowledge that three new states have developed nuclear capability (and Iran is soon to join them, apparently) after the United States signed but did not ratify the Comprehensive Nuclear-Test-Ban Treaty (CTBT). Furthermore, the Stockpile Stewardship Program has not shown that our weapons are reliable, because its conclusions are based on simulations that have never been checked by direct testing.

If the United States ratifies the CTBT, how will we or anyone know that our stockpile is reliable in decades hence? Simulations and limited lab experiments provide some data but are not definitive. As history shows,

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the CTBT does not slow those who join the nuclear club for reasons of their own. Tactical weapon reliability is the hardest to judge without tests, and may well be the most likely to be used. Ignoring this is folly.

It is also folly to imagine that total nuclear disarmament is stable—it is far too easy to cheat, even with no testing.

GREGORY BENFORD

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Response

I DID NOT CLAIM THAT THE COMPREHENSIVE Nuclear-Test-Ban Treaty (CTBT) will "bring nuclear peace," as Benford suggests. The CTBT is one step toward a nuclear weapon–free world. Others will be required, and each must promote stability and be verifiable. The process depends on a benefit-risk calculus of how best to ensure security.

Of the three states that have tested most recently, India and Pakistan did so in 1998, and only North Korea (in 2006 and 2009) did so after the Senate voted against the CTBT. In each case, it is arguable that prior U.S. ratification would have influenced the decision to test, particularly if U.S. ratification had led to ratification by China and others.

Benford claims that a direct (nuclear) test is necessary to ensure weapon reliability. This is not the case. Since 1996, the Stockpile Stewardship Program has been the basis for an annual certification of confidence in the reliability of nuclear weapons, both strategic and tactical (there are no technical differences between them that would affect confidence), without testing. The April 2010 Nuclear Posture Review foresees no future need for nuclear testing for maintaining such confidence, a position that the directors of the three nuclear weapons laboratories have endorsed (*1*). The Stockpile Stewardship Program has no direct correlation to constraining testing by potential adversaries, whereas the CTBT does. Such testing, and its damage to global stability, is not in the U.S. interest.

PIERCE S. CORDEN

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CORRECTIONS AND CLARIFICATIONS

Special Section on Scaling Up Alternative Energy: News: "Sending African sunlight to Europe, special delivery" by D. Clery (13 August, p. 782). The figure 12,000 gigawatts, cited as the amount of concentrating solar power needed to meet Europe's energy demand by 2050, in fact refers to worldwide demand.

Special Section on Scaling Up Alternative Energy: News: "Energy's tricky tradeoffs" by A. Cho (13 August, p. 786). The units for the map of average daily sunshine in the United States should be kilowatt-hours per square meter, not kilowatts per square meter.

Table of Contents: (16 July, p. 251). The one-sentence summary for the Report by C. K. Savile *et al*. was incorrect. The correct summary is "An engineered enzyme offers substantial efficiency advantages in the production-scale synthesis of a drug."

Reports: "Single-crystal x-ray structure of 1,3-dimethylcyclobutadiene by confinement in a crystalline matrix" by Y.-M. Legrand *et al*. (16 July, p. 299). The parent host structure G_4C and related solvent-inclusion compounds were reported recently: Y. Liu, M. D. Ward, *Cryst. Growth Des*. **9**, 3859 (2009).

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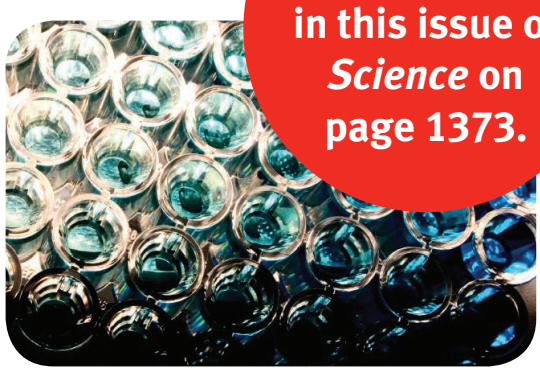

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INTERNET AND SOCIETY

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Jonathan Smallwood

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by Nicholas Carr
Norton, New York, 2010. 288 pp. $26.95, C$33.50. ISBN 9780393072228.

In *The Shallows*, writer Nicholas Carr explores the complex relationship between technology, society, and the mind. At the most basic level, technological advances are the vehicle through which intelligence drives societal change. A good example is the wheel. Sometime during human prehistory, the invention of the wheel allowed goods to be moved in a more efficient manner and so opened up new markets for Neolithic merchants. Look a little deeper, and it becomes obvious that the adoption of the wheel had a subtle secondary effect. In pre-wheel societies, it would have been common for goods to be carried on the back of a person or animal; after the development of the wheel, carts (and eventually trains and automobiles) removed this need. In addition to driving economic growth, the wheel engendered a more sedentary society. The invention of the wheel marked the beginning of a technological trajectory that culminated in today's obesity epidemic and, through our reliance on petroleum, the threat of global warming.

This bidirectional link between physical technology and society seems straightforward, but Carr focuses on sociological changes, such as writing, that alter our thinking. The invention of the written word allowed the creation of physical as opposed to mental records and so revolutionized how information was stored and shared. No longer was it necessary to memorize cultural knowledge in the form of songs or poems; the information could be directly recorded on clay, papyrus, or paper. As Carr points out, in order for societies to gain the maximum benefit from written words, people need to be able to read. Thus the development of written language went hand in hand with a cognitive shift toward the concentrated and serial linguistic thought that is necessary for reading. Over time, advances in writing beget changes in cognition, a process that has led to the high levels of literacy we see today. With technologies such as the book, our minds can achieve a higher state of consciousness than without them.

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As was the case for books, the development of the Internet has had a powerful influence on the way we think. We are familiar with this fact in a quite trivial sense: In today's world of Google and Wikipedia, one hardly needs to be able to remember anything at all. Instead, a query to Google can, in a matter of seconds, provide a detailed array of information on almost any topic. Coupled with instantaneous online access (through iPhones, Blackberries, and the like) from almost any corner of the globe, the Internet puts a vast storehouse of human knowledge within easy reach, whenever and wherever we are. Moreover, the influence of the Internet also has a vibrant social component. Sites such as Facebook allow us to maintain social groups that far exceed the size of those in pre-Internet society, while e-mail and Skype allow us to contact other members of our groups at a moment's notice.

Although the Internet has placed so much of humanity and its knowledge literally at our fingertips, there is no such thing as a free lunch. Carr's radical message is that the volume of content that we can access is increasing with a trajectory that outstrips even the most optimistic rates of evolutionary change for the physical matter of our brains. Carr argues that faced with this blizzard of content, we can no longer engage in detailed and thoughtful analysis. Rather, the rapid expansion in information has been accompanied by an increasingly superficial level of analysis. Confronted by more information than we can comfortably deal with, our minds are responding in the only way they can—by processing the immense stream in an increasingly shallow manner.

Carr also proposes that the Internet's influence on our cognition is amplified by its design. One of Google's stated aims is to make knowledge as accessible as possible. In sharp contrast to authors such as Tolstoy or Steinbeck who demanded studious attention from their readers, the Internet aims to deliver an information fix with minimal effort. Possibly more problematic, advertising revenue is the economic basis behind the Internet. Search engines are not only experts in providing content, they are also experts in what we want. Thus when delivering answers to our searches, Google also presents individually tailored advertisements in the most pertinent, eye-grabbing locations. Carr speculates that unlike books, which yielded cultural change that emphasized concentration and disciplined thought, the Internet (either by design or accident) is creating a society that specializes in the superficial.

Will Carr's vision of the future be proven correct? Is Facebook the beginning of the end for our species's remarkable ability to engage in complex, deep thought? Or is Google the path we will follow to become enlightened members of the cybergeneration? At the moment it is too early to say: Sociological changes (even those driven by rapidly improving technologies such as the Internet) take time. And the evidence that Carr discusses is often anecdotal or does not provide the clear and crisp answers that the question demands. What cannot be doubted is that the Internet is changing how we think and that the changes include subtle features that are often absent from the tweets of the Facebook generation. To help you answer the questions yourself, you might consider reading *The Shallows* somewhere quiet (ideally with your iPhone switched off)—if Carr is correct, online versions are probably best avoided.

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POLITICAL PHILOSOPHY

Arguing for the Achievable

Ken Binmore

Amartya Sen is one of the world's leading public intellectuals. He was awarded the Nobel Prize for Economics in 1998 for his theoretical work on the ethical dimension of economics. Through his research, his many books, and his teaching at Harvard University and elsewhere, he has tirelessly promoted the cause of the poor and the needy around the world. His practical contributions to the relief of suffering are such that in some parts of the world he is regarded more as a saint than an academic.

The Idea of Justice, Sen's latest book, seeks to explain why his brand of ethics should be preferred to that of rival moral philosophers. Two extracts from the chapter "Happiness, Well-Being and Capabilities" will serve to summarize his approach.

> [I]f someone has the power to make a difference that he or she can see will reduce injustice in the world, then there is a strong and reasoned argument for doing just that (without having to dress all this up in terms of some imagined prudential advantage in a hypothetical exercise of cooperation).

> I will concentrate … on the relevance of capability in the assessment of personal states and advantages, in contrast with the perspective of happiness emphasized in traditional welfare economics.

The first sentence promises to explain why the powerful have an obligation to relieve the suffering of the less fortunate. I am one of those who have sought to use evolutionary game theory to explain our sense of fairness (*1*), and so it is a disappointment to find no science at all in Sen's book: no appeal to evolutionary biology, no anthropological field data, no experimental psychology, and no behavioral economics. Nor is there any reliance on traditional philosophical arguments intended to show that ethical laws are somehow objectively binding irrespective of any scientific facts. Objectivity is said instead to be whatever an intellectual community of reasonable folk can be persuaded to endorse. Scholars (like such notable utilitarians as Peter Singer or Nobel Prize winner John Harsanyi) who are unmoved by quotations from Buddha or the Hindu scriptures can then presumably be ignored as being unreasonable. However, Sen is much less particular in the latter part of the book, where he discusses at length the virtues of public scrutiny within a modern democracy.

Themis (Auburn, Washington, Justice Center).

The Idea of Justice
by Amartya Sen
Harvard University Press, Cambridge, MA, 2009. 496 pp. $29.95, £22.95, €27. ISBN 9780674036130.

The second part of the first sentence quoted above is a reference to the traditional literature on ideal or utopian societies that begins with Plato's *Republic* and flourished most recently in John Rawls's *A Theory of Justice* (*2*). Sen admires Rawls (widely regarded as the leading moral philosopher of the past century) but regards the approach he represents as impractical on the entirely sensible grounds that knowing what would be best in an ideal world does not tell you which of two practical reforms are better.

The second quoted sentence introduces Sen's own theory of capabilities, which he advocates using to determine how to judge the quality of lives that need to be compared. Roughly speaking, Sen believes that we should seek to expand the set of opportunities available to those trapped at the bottom of the heap—a view with which I imagine few would disagree. However, it is disingenuous to suggest that the leading alternative is to seek to measure welfare in terms of "happiness." The modern economic theory of utility abandoned such psychological trappings more than 50 years ago. Nor is it true that rational choice theorists all believe that human beings are intrinsically selfish.

This would have been a better (and much shorter) book if Sen had not sought to dress up his ideas so as to appeal to the philosophical establishment. My guess is that those outside this charmed circle will be left cold by Sen's theoretical arguments but nevertheless agree wholeheartedly that there is no need for everybody to endorse some particular ethical theory in order to make the world a fairer place. All that is necessary is that enough people sufficiently near the levers of power should agree that it is worth cooperating on implementing a particular reform. Sen's theory of capabilities may not be the theoretically ideal way of evaluating reforms, but so what? If my hand were anywhere near a lever of power, I would be delighted to pull it on his behalf. As things are, one can only stand back and admire how many levers he has been able to pull himself.

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BROWSINGS

Cremona Violins: A Physicist's Quest for the Secrets of Stradivari. Kameshwar C. Wali. World Scientific, Singapore, 2010. 176 pp. + DVD. $55, £38. ISBN 9789812791092. Paper, $39, £27. ISBN 9789812791108.
The author describes the efforts of William F. Fry (a high energy physicist) to understand the source of, and duplicate, the sounds of instruments crafted by Amati, Bergonzi, Guarneri, and Stradivari. Early chapters introduce the 17th- and 18th-century violinmakers of Cremona, Italy; discuss the physics of sound production in violins; and sketch the history of violin research. Recognizing that accurate calipers and a scraping device were Stradivari's major tools, Fry developed techniques for making predictable acoustic changes after the violin is constructed. In an accompanying video, he demonstrates how fine-tuning the thickness gradations of the top plate enables him to reproduce the highly desired tonal qualities.

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DEMOGRAPHY

Remeasuring Aging

Adjusting aging forecasts to incorporate increases in longevity and health can provide better tools for policy-makers.

Warren C. Sanderson[1,3]* and Sergei Scherbov[2,3]

Population aging is an international concern, in part because of consequences of coming age-structure changes, e.g., growth in the number of elderly, decline in the number of youth, and accompanying economic and social costs (*1*–*4*). These expectations are based on conventional measures of aging that link expected phenotypes to fixed chronological ages. But as life expectancies increase and people remain healthy longer, measures based solely on fixed chronological ages can be misleading. Recently, we published aging forecasts for all countries based on new measures that account for changes in longevity (*5*–*8*). Here, we add new forecasts based on disability status. Both types of forecasts exhibit a slower pace of aging compared with the conventional ones.

Limits to Chronological Age

One advantage of aging forecasts based on fixed chronological ages (*1*, *9*, *10*) is that the United Nations (UN) computes them consistently for all countries of the world. These include the proportion of the population 65 and older, and the old-age dependency ratio (OADR), which considers people dependent upon others when they reach the age of 65 (often calculated as the number of people aged 65 or older, divided by the number of people of working age, 15 or 20 to 64). When using indicators that assume fixed chronological ages, it is implicitly assumed that there will be no progress in important factors such as remaining life expectancies and in disability rates. But many age-specific characteristics have not remained fixed and are not expected to remain constant in the future (*11*). In 1950, for example, 65-year-old women in Canada, Sweden, and the United States could expect to live an average of around 15 more years. By 2000, that had risen to about 20 (*12*), and the UN foresees further increases. Other forecasts also assume continuation of trends in life expectancy growth seen in the last decades (*8*, *13*), although the UN forecasts assume that the speed of life expectancy increases will slow.

Disability-free life expectancies, which describe how many years of life are spent in good health, have also been increasing, often as fast as unconditional life expectancies, because of decreases in age-specific disability rates (*14*). For example, in the United States, the proportion disabled in the age group 65 to 74 declined from 14.2% in 1982 to 8.9% in 2004–05 (*15*). Thus, fixed chronological ages do not work well in evaluating the effect of age structure changes on health care costs, because most of those costs occur in the last few years of life, which happen at ever later ages as life expectancies increase (*16*, *17*).

Life-Expectancy Adjustments

Defining old age by using life expectancy instead of chronological age was first suggested in (*18*), and expanded upon in (*19*). The more general point that ages could be adjusted for life-expectancy change much as financial variables are adjusted for inflation appeared first in (*20*). Forecasts of aging that take life expectancy into account are relatively easy to compute, but several issues contributed to their remaining underexplored. For example, concern about aging was less a priority until relatively recent years. And before publication of (*21*), life-expectancy adjustments were not available in a consistent format for all countries, and people were not trained in their use.

Alternative measures that account for life-expectancy changes show slower rates of aging than their conventional counterparts (*5*, *8*, *21*). For example, an alternative to the OADR is the prospective old age dependency ratio (POADR, defined as the number of people in age groups with life expectancies of 15 or fewer years, divided by the number of people at least 20 years old in age groups with life expectancies greater than 15 years). Effects of aging are evident in both measures, but when forecasted increases in life expectancy are taken into account, the POADR increases less rapidly than the OADR (see the table). Similar patterns are seen for many countries of the world (table S1).

Disability Adjustments

Disability-adjusted aging measures are another alternative [e.g., (*22*, *23*)]. But consistent disability-adjusted aging measures from many countries have not previously appeared in the literature. To investigate the effects of disability, we define a measure analogous to OADR, the adult disability dependency ratio (ADDR, defined as the number of adults at least 20 years old with disabilities, divided by the number of adults at least 20 years without them) (see the table and table S1).

Forecasting Dependency of the Elderly Population

	Old-age dependency ratios (OADR)			Prospective OADR (POADR)			Adult disability dependency ratios (ADDR)		
	2005–10	2025–30	2045–50	2005–10	2025–30	2045–50	2005–10	2025–30	2045–50
Switzerland*	0.27	0.41	0.48	0.15	0.18	0.24	0.09	0.10	0.11
Czech Republic	0.23	0.36	0.52	0.20	0.26	0.29	0.08	0.09	0.10
Germany	0.33	0.48	0.63	0.21	0.25	0.34	0.12	0.13	0.15
France	0.28	0.44	0.51	0.18	0.21	0.24	0.09	0.10	0.11
United Kingdom	0.27	0.36	0.41	0.19	0.20	0.22	0.10	0.10	0.10
Hungary	0.26	0.34	0.48	0.25	0.28	0.31	0.21	0.22	0.23
Italy	0.33	0.45	0.68	0.20	0.23	0.31	0.10	0.11	0.12
Japan*	0.35	0.55	0.78	0.18	0.27	0.29	0.10	0.12	0.13
Sweden	0.30	0.40	0.44	0.19	0.23	0.23	0.08	0.09	0.09
United States*	0.21	0.34	0.38	0.13	0.17	0.20	0.09	0.10	0.10
Average	0.28	0.41	0.53	0.19	0.23	0.27	0.11	0.12	0.12

*A country not in the EU-SILC survey.

Dependency ratios. Authors' calculations. OADR and POADR are based on (*11*). ADDR based on (*11*) and (*28*). The lower age boundary in all denominators is 20. See SOM §1 and tables S1 and S2 for more detailed methods and additional countries.

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The OADRs increase much faster than the ADDRs. In the United Kingdom, for example, the OADR increases from 0.27 in 2005–10 to 0.36 in 2025–30 to 0.41 in 2045–50. In contrast, the ADDR stays constant at 0.10. Although the British population is getting older, it is also likely to be getting healthier, and these two effects offset one another. Not only does the ADDR increase less rapidly than the OADR, it also increases less rapidly than the POADR, so that adjusting for the likely future path of disability rates does not simply replicate the results of adjusting aging measures for changes in longevity.

In our forecasts for the United States, in 2003 the number of expected years of disability above age 65 is 4.1. This finding differs slightly from (*22*), which forecast that figure to be 3.7 years in 2022. If the number of years of disability were forecast to change as in (*22*), the increase in ADDRs would be even less.

Previous forecasts were made for years 2003 to 2030 of the number of people 65 and older with severe disabilities for 12 countries of the Organization for Economic Cooperation and Development (OECD) from data that were not harmonized across countries (*23*). Constant age- and sex-specific disability rates were applied to future populations, and the trend in age- and sex-specific disability rates between two recent surveys was extrapolated. However, age- and sex-specific disability rates are changing, and trends between two surveys taken only a few years apart can be misleading, especially in the case of age- and sex-specific disability rates, because of the noisiness of those data.

Making consistent multicountry forecasts of the disability rates underlying the ADDR was difficult in the past. Data with a consistent measure of disability, harmonized across countries, were lacking. Data available for only one country, with disability-adjusted forecasts based on self-evaluated definitions of health, could reflect cultural specificity. The European Union Statistics on Income and Living Conditions survey (EU-SILC) survey now provides harmonized data on a specific definition of disability based on activity limitations [supporting online material (SOM) §2] for a large enough set of countries. A forecasting methodology was also needed that accounted for long-term relations between disability rates and mortality rates, and relations of disability rates across ages and sexes (SOM §1).

Even with the EU-SILC data, there are still problems. The EU-SILC could be biased if it systematically omits older people with disabilities. The survey does not include people in nursing homes (SOM §3.2 shows that this has little effect). In addition, we can currently only make disability-adjusted aging forecasts for high-income OECD countries, although we feel that this is sufficient to illustrate the potential advantages of the approach.

Better Tools for Policy-Making

Policy analysts long had little choice but to use aging forecast measures (e.g., published by the UN) based on chronological age. More recently, however, measures have been developed that do not assume that improvements in health and longevity will cease. These measures are not just different metrics for measuring the same thing. They measure different aspects of aging, ones in which biological and behavioral factors play a larger role. Other perspectives on aging are also possible, for example, in terms of prevalence of chronic diseases or of frailty, but these would also require new measures that are not based on chronological age.

The figures presented here are based on UN forecasts of survival rates. But populations are heterogeneous, and how this heterogeneity is treated influences how survival rates are forecast (*24*). Uncertainty in our forecasts comes primarily from two sources, (i) life-expectancy forecasts and (ii) disability rates that are conditional on those forecasts. But ADDRs are rather robust to differences in the speed of forecast life-expectancy changes and thus fairly insensitive to how heterogeneity is treated in making those forecasts (SOM §3.1). Use of ADDR could thus limit the scope for political speculation and controversy.

Such new measures of aging can help educate the public about likely consequences of improvements in health and longevity. Slow and predictable changes in pension age, for example, justified by an increased number of years of healthy life at older ages, may be more politically acceptable than large, abrupt changes justified on the basis of budgetary stringency. In 2000, the normal retirement age in the United States was 65. Today, it is 66; current legislation has it increasing to 67 in 2027 (*25*); and it is likely to increase further to help avoid reductions in future pension payouts. In the United Kingdom, the normal pension age is scheduled to rise from 65 to 68 by 2044 (*26*) and in Germany from 65 to 67 by 2031 (*27*). A change in U.S. legislation, for example, that would increase the normal pension age by one-half year for each year of additional life expectancy at age 65 would go a long way to ensuring the sustainability of Social Security payouts, even without further reforms. People who enjoy longer lives would finance part of their additional years of retirement themselves.

Population aging will certainly be the source of many challenges in coming decades. But there is no reason to exaggerate those challenges through mismeasurement. We will be able to address those problems better with a larger array of measures of aging, using those that are appropriate to the task at hand.

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CELL BIOLOGY

Septins at the Nexus

Yves Barral

The ability of a cytoskeletal protein to prevent membrane protein diffusion is important for cilia formation and maintenance.

Eukaryotic cells exist in a wide variety of shapes and functions. A source of variability is the appendages that cells form on their surfaces, such as the spines and axon that a neuron extends, the motile flagella of sperm and protists, and the beating cilia that many animal cells bear. These appendages constantly exchange material and information with the cell body from which they project, while maintaining their individuality. How they form and maintain themselves has intrigued scientists for almost a century. A study by Kim *et al*. (*1*) on page 1337 of this issue, and another by Hu *et al*. (*2*), report how proteins called septins contribute to the formation and maintenance of vertebrate cilia.

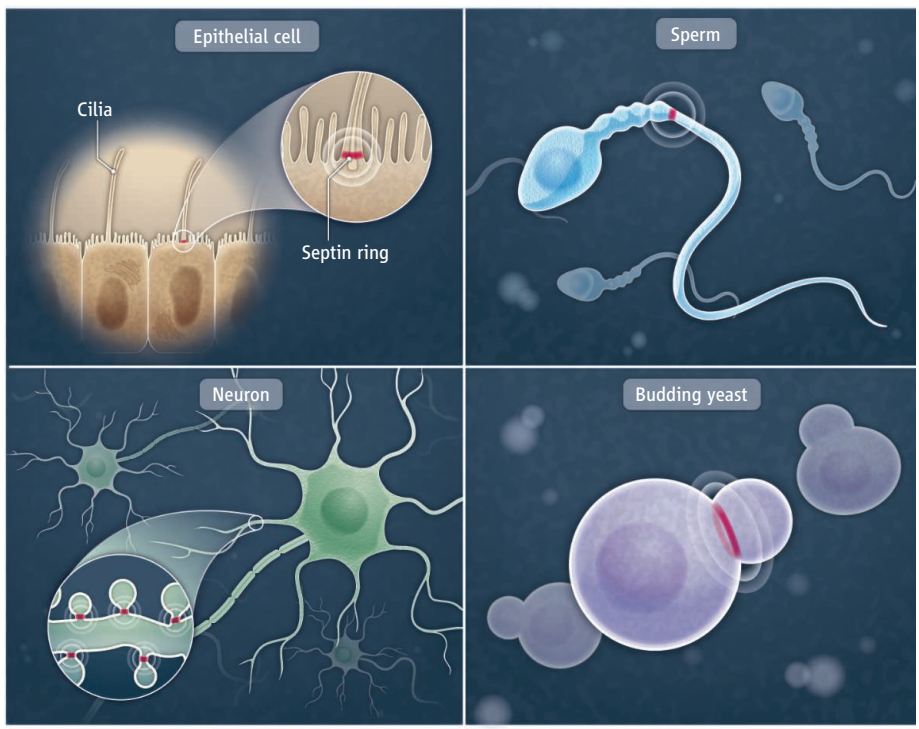
Cilia form on nondividing animal cells upon recruitment to the cell cortex of a cytoskeletal (microtubule) structure called the centriole. The centriole matures into a basal body that assembles an axoneme, the microtubule shaft of the cilium. In many metazoa, cilium formation is controlled by planar cell polarity, a signaling pathway that ensures that in sheets of cells all cells orient along the same axis. Vertebrate cilia act in many cellular and developmental processes including the establishment of right-left body asymmetry (*3*, *4*). Indeed, mutations in ciliary proteins are implicated in numerous disorders (ciliopathies), including cystic kidney diseases, mental retardation, obesity, and blindness. Moreover, at least in the fly *Drosophila melanogaster*, the only essential function of centrioles is cilia formation (*5*).

Kim *et al*. and Hu *et al*. show that members of the septin family of guanosine triphosphatases (GTPases)—SEPT2 (in mammalian cells) and Sept2 and Sept7 (in frog cells)—form a ring at the base of cilia. There, it induces the formation of a barrier, compartmentalizing the plasma membrane, and preventing membrane proteins from laterally diffusing out of the cilium. Both studies show that a lack of septin expression impairs ciliogenesis in vertebrates.

Septins assemble into multimers and form nonpolar filaments (*6*). Filament assembly is stimulated by septin interaction with the membrane component phosphatidyl inositol polyphosphate and affects the organization of underlying membranes (*7*, *8*). Using an optical technique (fluorescence recovery after photobleaching) to track the movement of fluorescent reporter membrane proteins (in mammalian cells), Hu *et al*. show that septins insulate the ciliary membrane from the plasma membrane. When reporter proteins located in the ciliary membrane were photobleached, no fluorescence recovery was observed (during the 10 min of the experiment), indicating that the photobleached molecules, which diffuse at the surface of the cilium, did not exchange with still-fluorescing proteins from the remainder of the cell membrane. By contrast, cells with a reduced amount of SEPT2 (that still bear a cilium) did recover fluorescence, indicating that confinement of ciliary proteins to the ciliary membrane was impaired. Thus, Hu *et al*. establish that septins contribute to barrier formation at the base of the cilium. Furthermore, in cellular fractions, SEPT2 purified with membranes and not the basal body, which showed that septins contributed to cilium formation by acting on its membrane.

How is recruitment of septins at the right time and place achieved to support ciliogenesis? Kim *et al*. show that in frog cells, Sept2 and Sept7 directly interact with the signaling protein Fritz and mediate many, if not all, its effects in planar cell polarity including ciliogenesis. The control of its function by planar polarity confirms that septin must act early in ciliogenesis. Moreover, Fritz and septins were interdependent for localization. Thus, Fritz is a component of the septin complex during ciliogenesis, specifying septin's role in this process. The authors also show that mutations in the human Fritz protein correlate with clinical variants of the human ciliopathic disorders Meckel-Gruber and Bardet-Biedl syndromes. Given the connection between Fritz and septins, it is probable that septin mutations are also involved in these disorders.

Kim *et al*. and Hu *et al*. both show that septin defects impact signaling by the secreted molecule Hedgehog (Hh). Hh controls many processes during vertebrate embryonic development and in the adult. In primary cilia, Hh receptors must localize to the ciliary membrane to function. Lack of functional septin causes their diffusion out of this location and thus impairs signaling. Why the receptor needs to be in the ciliary membrane to signal



Barrier rings. A ring of septin protein assembles at the base of the cellular appendages shown, creating a barrier that restricts the diffusion of membrane proteins.

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is not yet fully understood.

In the past few years, mammalian septins have been found at the neck of dendritic spines and at the base of sperm flagella (*9*–*12*). In both cases, a lateral diffusion barrier is present at these locations. In budding yeast, septins govern the compartmentalization of membranes, restricting the exchange of cellular material between mother and bud. Thus, reports of Kim *et al*. and Hu *et al*. confirm the emergence of septins as conserved players in the assembly of diffusion barriers at the bases of cellular appendages in eukaryotes (*13*) (see the figure). This suggests that many apparently different appendages might have the same evolutionary origin. It will be important to determine how septins contribute to the formation of diffusion barriers and how these barriers function.

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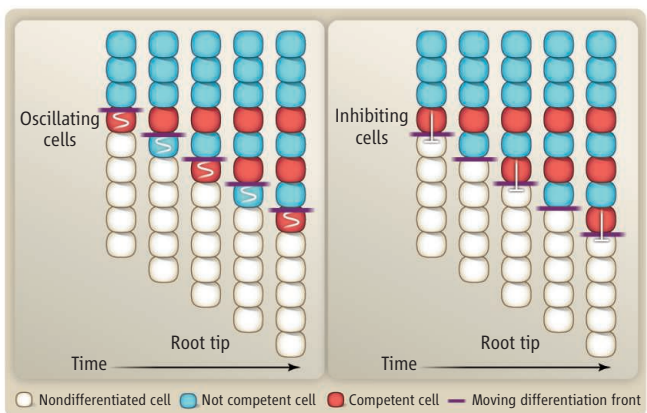
PLANT SCIENCE

Oscillating Roots

Where plant roots branch may be decided by rhythmic pulses of gene expression.

Jan Traas and Teva Vernoux

During embryo formation in higher plants, only a rudimentary body forms, consisting of an embryonic root, a stem, and a limited number of leaves. The rest of the plant, including its extensive network of branching roots and stems, is derived from two populations of stem cells at the tips (meristems) of the embryonic root and shoot. The developmental mechanisms that control this branching, however, have been unknown. On page 1306 of this issue, Moreno-Risueno *et al*. (*1*) demonstrate that cyclic expression of genes in root meristems can generate the elaborate network of branching roots that anchors the plant and provides it with essential nutrients.



Two possible routes to roots. Left: Nondifferentiated cells (white) start to oscillate following an internal clock. When the differentiation front (purple) reaches these cells, they stop oscillating. Depending on the phase of the cycle when the cell stops oscillating, it will be competent (red)—capable of forming lateral roots—or not (blue). Right: The same result could be produced if competent cells (red) inhibit newer, adjacent cells from becoming competent. Note: Circles represent in principle groups of cells.

The work of Moreno-Risueno *et al*. rests on previous observations suggesting that genes in cells close to the meristem show an oscillating sensitivity to the plant hormone auxin and could be involved in determining the locations where roots branch laterally (*2*, *3*). To investigate this idea, they used a promoter, DR5, that appears to be sensitive to auxin levels, with a luciferase gene that "lights up" when activated; this coupling allowed the researchers to detect changes in DR5 activity in real time. They observed that expression of DR5 pulsed rhythmically about every 6 hours in a zone a short distance from the root tip. This activity, however, seems to represent just the tip of an iceberg, as an analysis of gene expression levels in this so-called oscillation zone (OZ) showed massive changes affecting almost 3500 genes that fluctuated in or out of phase with DR5.

The picture that emerges is as follows: As the root meristem continuously produces undifferentiated cells as it grows, the OZ follows behind the tip at a more or less fixed distance. When new cells enter the OZ, the gene network starts to oscillate until the cells exit the zone and enter differentiation. A cell that exits the OZ during a certain phase of the oscillation cycle will be competent, or capable of forming lateral roots.

This scenario, where changes in gene expression depend on the internal "clock" of every cell, is very different from what has been proposed for pattern formation at the shoot meristem. Here, competent cells appear to inhibit branching in adjacent cells. Changes in gene expression at the shoot apex, therefore, seem to depend on signaling between cells. The root scenario, however, is intriguingly similar to the one proposed for the formation of somites (body segments) in vertebrates (*4*, *5*). Cells of the presomitic mesoderm also show oscillating gene expression, involving genes of the Notch and Wnt signaling pathways. These oscillations are translated into spatial arrangements of segment boundaries, through a process implicating a gradient of the growth factor Fgf8, which decreases in more anterior cells where the differentiation process takes place. As growth continues at the tail end of the embryo, cells exit from the anterior end and cease oscillating, probably because the concentration of Fgf8 declines with the increasing distance from the tail bud. Depending on the phase of the oscillation cycle in which the cells become arrested, they switch on different sets of genes, marking them as the front or back end of the next somite. These oscillations are called the clock, and the moving differentiation front is called the wavefront; somite patterning thus depends on a clock-and-wavefront mechanism.

There seems to be, however, an important difference between the animal and plant systems. In a typical vertebrate, an individual cell will go through several oscillations. In a chicken, for instance, certain cells will sense up to 12 fluctuations before differentiation

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occurs (*5*). In contrast, the number of oscillations in the OZ of the root seems much more restricted. The study's figure does not provide cellular-level resolution, but known growth dynamics (*6*) suggest that, in the root, a single cell nucleus (or its descendants) will spend only a couple of hours in the OZ. This implies that it could go through as little as a single fluctuation between entering and leaving the OZ. If this is true, the genetic clock could tick several times in vertebrates, but just once in the root. This single fluctuation could be based on a vertebrate-like clock-and-wavefront system. Other mechanisms, however, could also generate a single fluctuation. For example, a scenario where more mature cells send signals back to cells in the OZ would produce a similar pattern (see the figure). To determine the exact mechanism, it will be important to define the number of oscillations every cell experiences. Because the root is readily accessible, such an analysis at the cellular level should be much easier to achieve than in animal systems.

Another question is whether auxin alone is responsible for the observed oscillations. Although the DR5 promoter is often considered to be a sensor of auxin levels, Moreno-Risueno *et al*. show that other auxin-responsive genes, such as *IAA19*, do not fluctuate in a similar manner. This observation implies that the fluctuations in DR5 activity do not necessarily depend on equivalent fluctuations in auxin. Unfortunately, it is currently impossible to visualize auxin directly, so it is difficult to determine to what extent changes in DR5 activity depend on hormone fluctuations alone. The results, however, strongly suggest that the competence to react to auxin is important, as is the cell's final response (*7*).

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MEDICINE

The Blood Stem Cell Holy Grail?

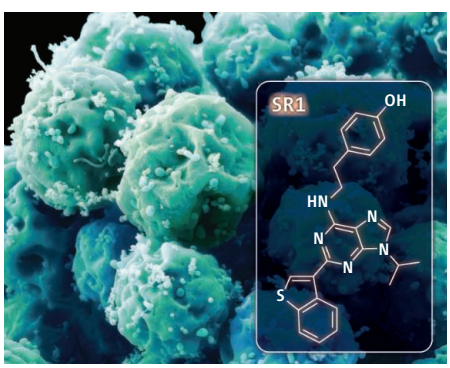
A compound promotes robust expansion of human hematopoietic stem cells in culture.

Guy Sauvageau[1,2] and R. Keith Humphries[3,4]

Hematopoietic stem cell (HSC) transplantation is one of the major medical discoveries of the 20th century. A recent worldwide survey indicated that in 2006 more than 50,000 HSC transplants were performed (*1*), saving tens of thousands of lives every year. Unfortunately, many patients in need of HSC transplantation are deprived of this life-saving procedure because of an insufficient number of stem cells in the graft, potentially leading to graft failure, a complication associated with a high mortality rate. This is a frequent problem in patients undergoing autologous (stem cells from one's own marrow) transplantation and in patients receiving an allogeneic (stem cells from a donor) transplant with HSCs derived from human cord blood. Recent clinical studies with cord blood grafts from different donors indicate that even a modest (two- to threefold) ex vivo expansion of HSCs would have a profound clinical impact. On page 1345 of this issue, Boitano *et al*. (*2*) report a major stride toward the goal of ex vivo expansion of human HSCs with their exciting discovery of a small molecule called StemRegenin1 (SR1) (see the figure).

The advance by Boitano *et al*. is the result of several bold steps that included screening a drug library of some 100,000 small molecules. Coupled with the ambitious scale of the screen, the authors developed an assay based on primary human hematopoietic cells enriched for primitive progenitors (cells purified from peripheral blood that express the cell surface antigen CD34) and a readout after 5-day culture to detect expansion in the number of stem/progenitor cells that continued to express CD34 (assessed by confocal immunofluorescence microscopy). This approach goes against the dogma that a screen with primary hematopoietic stem/progenitor cells, as opposed to hematopoietic cell lines, would be unworkable. In addition, it has long been held that cell surface markers would prove too unstable or unreliable to track expansion of HSCs under culture conditions. Not only did SR1 reproducibly expand $CD34^+$ peripheral blood HSCs, but it also greatly expanded the number of stem cells isolated from cord blood. Boitano *et al*. documented that treatment with SR1 resulted in a 17-fold net expansion in the number of cells capable of long-term hematopoietic repopulation when transplanted into immunodeficient mice, the current gold standard for detecting human HSCs. SR1 appears to skew primitive hematopoietic cells, including stem cells, toward self-renewal and away from differentiation.

Comparisons of gene expression changes induced by SR1 with a less active chemical variant revealed that the target of SR1 is the aryl hydrocarbon receptor (AhR). SR1 binds to, and is an antagonist of, this receptor, a ubiquitous ligand-activated transcription factor that induces the expression of drug-metabolizing enzymes. AhR is a member of the Per-ARNT-Sim superfamily of proteins that initiate intercellular signaling upon sensing extracellular toxic molecules such as tetrachlorodibenzo-p-dioxin (TCDD), a polyhalogenated and mutagenic environmental pollutant of the dioxin family. AhR localizes to the cytoplasm, coupled to molecular chaperones such as hsp90 (*3*). Exposure to dioxins triggers the migration of AhR to the nucleus, where it heterodimerizes with the aryl hydrocarbon receptor nuclear translocator [ARNT, also known as hypoxia-inducible factor–1B (HIF-1B)]. This dimer then binds to a consensus AhR response element present in genes that



Expansion enhancer. The compound SR1 promotes the self-renewal of human hematopoietic stem cells in culture. SR1 is an antagonist of the aryl hydrocarbon receptor.

PHOTO CREDIT: STEVE GSCHMEISSNER/ALAMY

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may regulate hematopoiesis, including those that encode the transcription factors c-Myc and HES, and CCAAT/enhancer binding protein (C/EBP) (*3*–*5*). Accordingly, agonists of AhR such as TCDD compromise HSC activity in mice (*6*), whereas Boitano *et al*. found that antagonists such as SR1 enhance expansion of human HSCs.

Curiously, SR1 is not active against the mouse AhR but is active against that of dog and monkey. These species-specific activities are consistent with the observed effect, or lack thereof, in stimulating ex vivo expansion of HSCs from these species and suggest the need for developing screens with human target cells.

It will be critical to define the cell population that responds best to SR1. Several types of mouse HSCs, some with short- and long-term repopulation potential, have been described (*7*, *8*). Serial transplantation experiments performed by Boitano *et al*. indicate that SR1-exposed cells can repopulate mice up to several months while preserving their multilineage potential, thus showing intermediate repopulation potential. The development of new reagents and better assays for analyzing pure subsets of human HSCs will be essential to address this clinically relevant issue.

Other molecules such as TAT-HOXB4 (*9*), TAT-NF-Ya (*10*), Notch ligand (Delta$^{ext\text{-}IgG}$) (*11*), pleiotrophin (*12*), and angiopoietin-like molecule 2 and 3 (*13*) enhance human hematopoiesis in immunocompromised mice. However, none of the reported effects are as robust as that of SR1. Moreover, in some cases (e.g., Notch ligand), engraftment was accelerated but the effect was transient, suggesting that more mature progenitors—as opposed to long-term HSCs—preferentially responded to the treatment. Combining treatments that enhance the activity of stem cells with long- and short-term repopulation potential may prove clinically beneficial.

A technology that expands human HSCs by orders of magnitude over what is now achievable with SR1 could rapidly pave the way for using stem cell transplantation to cure genetic diseases (gene therapy) or to protect stem cells from the deleterious effects of chemotherapy. But can human HSCs be expanded further, or have they achieved their limit once exposed to SR1 for several days or weeks? Mouse HSCs can be expanded by several thousandfold if genetically engineered to overexpress *Hox* genes and/or derivatives (*14*, *15*), and human HSCs should behave similarly once the basic molecular machinery underlying self-renewal is dissected. Although AhR has just entered the arena, it will rapidly become a key actor in this search for signaling pathways that determine HSC self-renewal. Equally important, AhR inhibition could lead to expansion of other adult-type stem cells (e.g., skin, gut, central nervous system). Are HSC transplant physicians about to lay their hands on the Holy Grail?

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CLIMATE CHANGE

Farewell to Fossil Fuels?

Barring new CO_2 sources could curb climate change, but won't solve energy problems.

Martin I. Hoffert

One concrete goal adopted by some policy-makers is to reduce the risks associated with climate change by preventing the mean global temperature from rising by more than 2°C above preindustrial levels (*1*). Climate models indicate that achieving this goal will require limiting atmospheric carbon dioxide (CO_2) concentrations to less than 450 parts per million (ppm), a level that implies substantial reductions in emissions from burning fossil fuels (*2, 3*). So far, however, efforts to curb emissions through regulation and international agreement haven't worked (*4*); emissions are rising faster than ever, and programs to scale up "carbon neutral" energy sources are moving slowly at best (*5*). On page 1330 of this issue, Davis *et al*. (*6*) offer new insights into just how difficult it will be to say farewell to fossil fuels.

The authors ask this question: What would future CO_2 levels and global mean temperatures be if humans built no additional CO_2-emitting devices (e.g., power plants, motor vehicles) and allowed existing CO_2-emitting devices to live out their normal lifetimes over the next 50 years? Their answer is that this strategy would limit mean warming to 1.3°C (1.1° to 1.4°C) above that of the preindustrial era and limit atmospheric concentrations of CO_2 to less than 430 ppm. They concede, however, that such a radical "age-out" scenario is unlikely, and that a major mobilization is needed to figure out how to power the world carbon-neutrally to stay below the 2°C threshold.

The bitter pill implicit in Davis *et al*. and other, earlier studies of emissions-reducing scenarios is that we are in no position to make this energy transition now, and that it will likely take decades of hard work (*7*). For example, Pacala and Socolow (*8*) analyzed a scenario that envisioned stabilizing atmospheric concentrations of CO_2 at 500 ppm within 50 years. They found that reaching that goal required the deployment of seven existing or nearly existing groups of technologies, such as more fuel-efficient vehicles, to remove seven "wedges" of predicted future emissions (the wedge image coming from the shape created by graphing each increment of avoided future emissions). Those seven wedges, each of which represents 25 gigatons of avoided carbon emissions by 2054, are cited by some as sufficient to "solve" climate change for 50 years (*9*).

Unfortunately, the original wedges approach greatly underestimates needed reductions. In part, that is because Pacala and Socolow built their scenario on a business as usual (BAU) emissions baseline based on assumptions that do not appear to be coming true. For instance, the scenario assumes that a shift in the mix of fossil fuels will reduce the amount of carbon released per unit of energy. This carbon-to-energy ratio did decline during prior shifts from coal to oil, and then from

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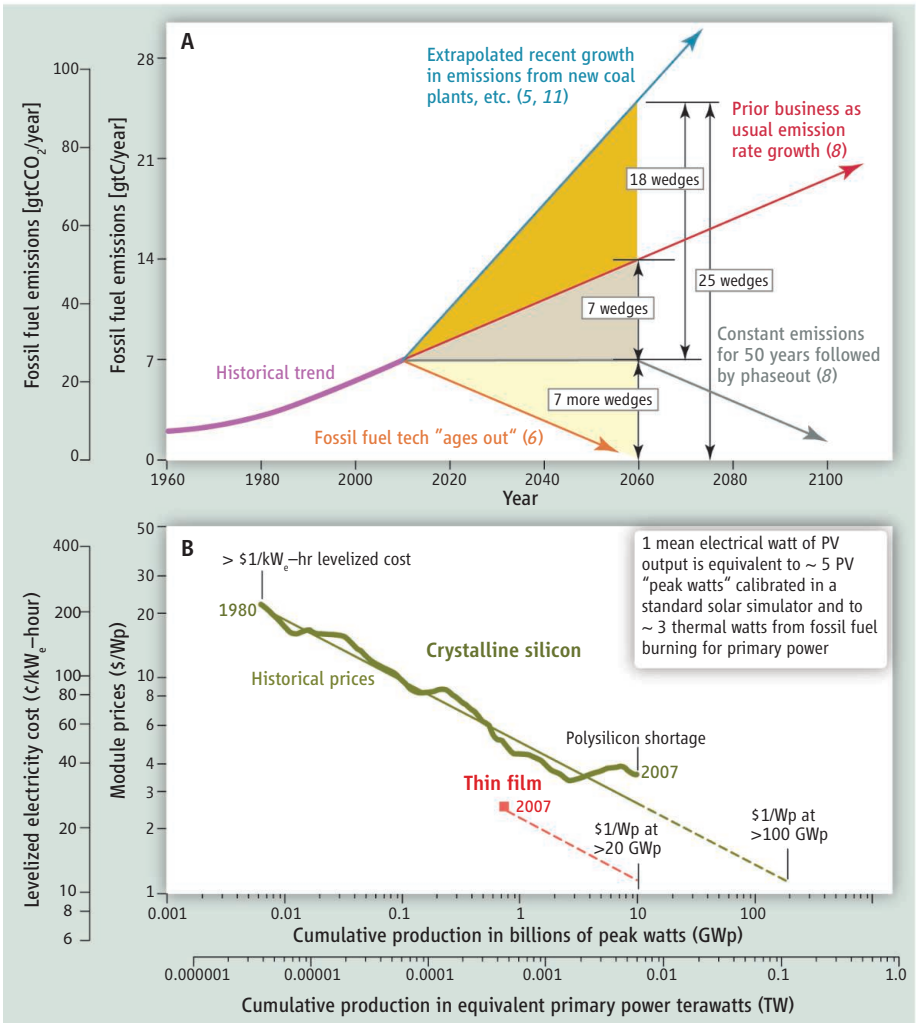

Reducing emissions. (**A**) Estimates based on one emissions scenario (red line) (*8*) found that technologies capable of removing 7 "wedges" of future predicted emissions could stabilize future CO_2 emissions from fossil fuels. Other scenarios (blue and gold lines) (*6*, *11*) suggest that removing up to 25 wedges will be needed. (**B**) Cost of producing electricity from silicon and thin-film photovoltaics (PV) are declining, but extensive development is needed to scale up cost-effective solar power to produce needed terawatts of primary power.

oil to natural gas. Now, however, the ratio is increasing as natural gas and oil approach peak production, coal production rises, and new coal-fired power plants are built in China, India, and the United States (*10*).

The enormous challenge of making the transition to carbon-neutral power sources becomes even clearer when emissions-reduction scenarios are based on arguably more realistic baselines, such as the Intergovernmental Panel on Climate Change's "frozen technology" scenario (*11*, *12*). Capturing all alternate energy technologies, including those assumed within this BAU scenario, means that a total of ~18 of Pacala and Socolow's wedges would be needed to curb emissions (*13*) (see the figure). And to keep future warming below 2°C, even under the Davis *et al*. age-out scenario, an additional 7 wedges of emissions reductions would be needed—for a total of 25 wedges (see the figure).

Maintaining world economic growth and keeping atmospheric CO_2 concentrations below 450 ppm, even with continuing improvements in energy intensity (the amount of CO_2 emitted per unit of energy, and a proxy for increasing energy efficiency and less consumptive lifestyles), will require ~30 terawatts (TW) of power from carbon-neutral sources at mid-century (*2*). Some forecasts envisioned market forces spurring the creation of 10 carbon-neutral terawatts (*2*), but that now appears optimistic. The difficulties posed by generating even 1 TW of carbon-neutral power led the late Nobel Laureate Richard Smalley and colleagues to call it the "terawatt challenge" (*14*–*16*); we have yet to mobilize enough talent and resources to meet it. It has proven difficut, for example, to tap the huge, if diffuse, solar flux on Earth using photovoltaic (PV) cells to generate electricity in a cost-effective manner, particularly for routine "baseload" generation. Costs of PV technologies are dropping (*17*) (see the figure), but greater economies of scale, perhaps accompanied by a switch to thin films—a less efficient technology, but less expensive in terms of cost per kilowatt—will help. Achieving massive market penetration of solar and wind electricity will require utility-scale systems that can store intermittent supplies of power until they are needed. Denmark, for instance, uses intermittent power to pump water into Norway's hydropower impoundments; the water is later released through turbines. That approach, however, isn't widely feasible in the United States, and other approaches that use compressed air, flywheels, and "flow batteries" to store power are expensive and need substantial research and testing.

Broad investment will be crucial to enabling such basic research findings to cross the "valley of death" and develop into applied commercial technologies. Carbon taxes (*1*) and ramped-up government research budgets (*2*) could help spur investments, but developing carbon-neutral technologies also requires, at the very least, reversing perverse incentives, such as existing global subsidies to fossil fuels that are estimated to be 12 times higher than those to renewable energy (*18*). We have to stop marching the wrong way before we can turn around.

Davis *et al*. show that breaking the world's fossil-fuel addiction will be hard. To create carbon-neutral power sources, we may well need programs with the scale and urgency of the Manhattan atom bomb project. One goal should be to develop technologies that can first meet the terawatt challenge, and eventually provide 30 carbon-neutral terawatts of power by mid-century; perhaps 10 TW each of primary power from "clean coal" and from nuclear and renewable technologies. Without these alternatives to fossil fuels, the age-out scenario painted by Davis *et al*. evokes Havana after the 1959 Cuban Revolution: no new cars, only constantly repaired but still running old Chevys in the streets, as a beautiful old city crumbles around them.

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MATERIALS SCIENCE

Shape Memory Bulk Metallic Glass Composites

Glass-forming and shape memory metals may provide a route to fabricating materials with enhanced mechanical properties.

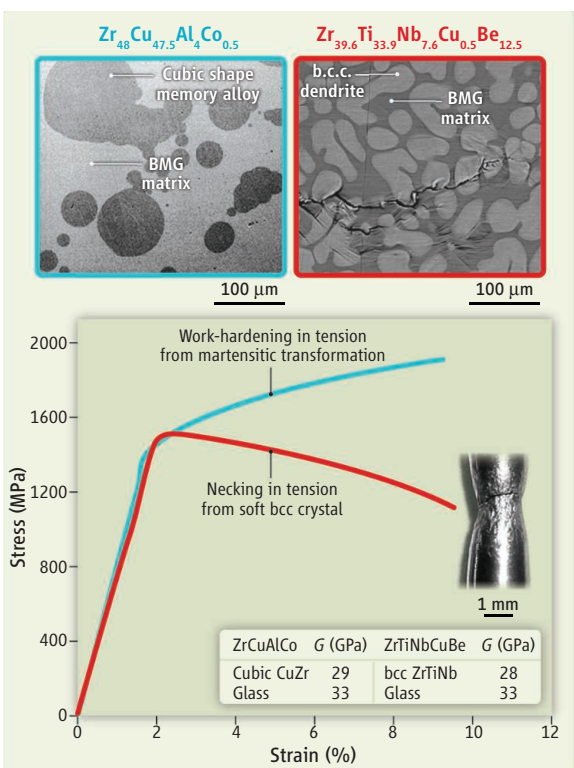
Douglas C. Hofmann

Bulk metallic glasses (BMGs) are being studied extensively as potential structural materials as they have a unique array of mechanical properties compared to traditional crystalline metals (*1*–*4*). Their amorphous microstructure and variable composition give BMGs ultrahigh-yield strengths, large elastic strain limits, high hardness, corrosion resistance, and the ability to be processed like a plastic. So far, however, BMGs have not found many structural applications because of their catastrophic failure under tension (tensile loading) and their typically low fracture toughness (resistance to cracking), both resulting from the same amorphous microstructure that differentiates them from crystalline metals. This shortcoming has been addressed in recent years with the development of BMG matrix composites (BMGMCs)—two-phase alloys consisting of soft, crystalline dendrites grown in situ in a glass-forming matrix (*5*–*9*). When designed and processed properly, BMGMCs retain the positive structural features exhibited by monolithic (single-phase) BMGs, but can also exhibit enhanced tensile ductility, fracture toughness, and fatigue endurance, which makes them desirable as engineering materials (*5*, *10*, *11*).

In conventional crystalline metals, strength and ductility are typically inversely proportional, a result of the interactions between dislocations and microstructural features, like grain boundaries. In contrast, BMGMCs exhibit plasticity through a complex interaction between the dislocations in the crystalline phase and the highly localized shear bands in the glass matrix. This results in mechanical properties (like fracture toughness) that exceed the "rule of mixtures" expected for each phase individually (*5*).

Dendrite-reinforced BMGMCs do exhibit some drawbacks, however. The two-phase alloy must contain a dendrite in thermodynamic equilibrium with a glass-forming liquid. This necessitates a system that has very sluggish crystallization kinetics, in order to prevent the dendrites from causing heterogeneous nucleation of unwanted brittle phases. This typically requires the use of Be-containing composites, which have very few stable compounds and are excellent glass-formers, but which require special consideration during processing owing to the toxicity of Be. Improvements in mechanical properties (e.g., tension ductility) have been confined almost exclusively to Zr-Ti-Be–based BMGMCs, which has limited the scope of applications.

Recent advancements in metallic glass composites come at the intersection between two different areas of materials science research—shape memory alloys and metallic glasses—whereby a shape memory alloy has been integrated as the crystalline phase, effectively using the concept of transformation-induced plasticity (*12*, *13*) (see the figure). The most widely studied shape memory alloy, NiTi (or Nitinol), undergoes a stress-induced martensitic transformation from a cubic to a monoclinic phase, which imparts an appreciable work-hardening capability (the alloy becoming stronger as it deforms). Less well known is that CuZr also exhibits the same shape-memory effect as NiTi. In a remarkable coinci-



Tensile ductility in metallic glass composites. (**A**) A scanning electron micrograph (SEM) from a CuZrAlCo composite showing the isolated shape memory alloy phase embedded in a glass matrix. (**B**) An SEM micrograph from a ZrTiNbCuBe composite showing isolated body-centered cubic (bcc) dendrites embedded in a glass matrix with a crack arrested by the microstructure. (**C**) Two tension tests representative of the work-hardening behavior observed in shape memory–reinforced composites and the necking behavior observed in bcc dendrite–reinforced composites. The shear modulus of the crystal and glass matrix of both composites is shown in the inset, demonstrating that the inclusion is a soft phase, one of the criteria necessary for tensile ductility.

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dence, the best binary metallic glass-former in the Cu-Zr system, $Cu_{50}Zr_{50}$, has the same composition as the shape memory alloy CuZr. When cooled rapidly, as is the case with Cu-mold casting, composites consisting of the cubic phase in a glass matrix can be obtained, even though the cubic-CuZr phase is thermodynamically stable only at high temperatures. This technique was originally demonstrated for a two-phase shape memory/metallic glass composite in $Cu_{47.5}Zr_{47.5}Al_5$ by annealing at high temperatures to partially crystallize the matrix into the cubic phase (*14*).

Aside from the mechanical properties, these new shape memory BMGMCs also crystallize into a softer phase than the metallic glass. In nearly every system observed, BMGs crystallize into a hard phase, typically an intermetallic, which makes them very brittle. Achieving ductility from a BMGMC requires that the crystal phase has a shear modulus lower than that of the matrix material, such that deformation is "attracted" to the inclusion (*6*). Until now, the only solution was to add a beta-stabilizer (Nb or V) to a dendrite-reinforced BMGMC. This technique, which has predominantly been applied to Zr-Ti-Be–based composites, usually results in an appreciable instability under tension. By partially crystallizing the BMG into a composite with a shape-memory phase, extensive work hardening can be achieved (see the figure). Under tensile deformation, shear bands that form above the yield strength in the glass matrix are arrested by the soft cubic phase, which then undergoes a martensitic transformation into the harder monoclinic phase. This causes a cascade of shear bands to form, which ultimately leads to tensile plasticity.

Shape memory–reinforced metallic glass composites greatly enhance the potential structural applications for amorphous alloys, in addition to opening up a new direction for scientific research. Future work requires controlling the nucleation and growth of the shape-memory phase so that the crystals are homogeneously distributed within a continuous glass matrix. Emerging commercialization for these materials includes energy-absorbing structures, biomedical implants, aerospace hardware, and sporting equipment.

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BIOCHEMISTRY

Exciting Structures

High-resolution structures of folding intermediates of proteins come into view.

Hashim M. Al-Hashimi

The beautiful images of protein structures that we see in journals and textbooks have contributed immensely to our basic understanding of how proteins fold and function. Yet these structures represent only one state of the protein—typically its most probable "ground state." Proteins, however, undergo dynamic excursions from their ground states and, much more rarely, morph into entirely different structural forms sometimes referred to as excited states. A growing number of studies suggest that excited states are a ubiquitous feature of biomolecules that may hold the key to unlocking some of the deepest and most poorly understood aspects of catalysis (*1*), signaling (*2*), recognition (*3*), and folding (*4*). It has proven to be a very daunting task, however, to determine the high-resolution structure of excited proteins using conventional techniques such as nuclear magnetic resonance (NMR) spectroscopy and x-ray crystallography. In part, this is because excited states exist for too little time (less than a millisecond) and in too little abundance (less than 5% of protein molecules). On page 1312 of this issue, Korzhnev *et al.* (*5*) outline a general strategy for overcoming these challenges using NMR data and computational methods. Their approach marks the meeting of two research frontiers that have successfully capitalized on the power of observing, in experiments, the "NMR chemical shift," an important electromagnetic characteristic of atoms in protein molecules.

Every NMR-active atomic nucleus has a characteristic resonance frequency (ω), referred to as chemical shift, which is exquisitely sensitive to its local structural environment and which appears as a peak in the NMR spectrum (see the figure). Although the transient nature of proteins in excited states often makes it impossible to directly observe their NMR spectra, under the right conditions they leave their mark by broadening the observable peaks of the ground state, even if their fractional population is as little as 0.5%. To understand this broadening, consider a nucleus in a protein that exchanges between a major ground (N) and minor (I) excited state with chemical shift frequencies, ω_N and ω_I. In the absence of exchange, one observes two NMR peaks, centered on ω_I and ω_N, with relative heights that reflect their populations (see the figure). Now consider what happens when N and I exchange on a time scale ($k_{ex} = k_{NI} + k_{IN}$) that is comparable to their differences in frequency ($\Delta\omega = \omega_N - \omega_I$), a condition satisfied by many but not all excited states. Each nucleus no longer has one well-defined observable frequency; rather, the frequency fluctuates between ω_N and ω_I. Because the fluctuation is stochastic, the same nucleus in different molecules spends varying amounts of time in the N and I state during the NMR experiment. This produces a range of observable frequencies, and the NMR peak is correspondingly broadened to reflect this range. Investigators can use a set of NMR experiments called "relaxation dispersion" to examine the broadening of a protein's ground state and thereby obtain the population, lifetime, and chemical shift of the otherwise invisible excited state (*6*, *7*).

The chemical shift of the excited state contains valuable information about its structure. Until recently, however, there was no way to uniquely and reliably translate the chemical shift data into a protein structure. Instead,

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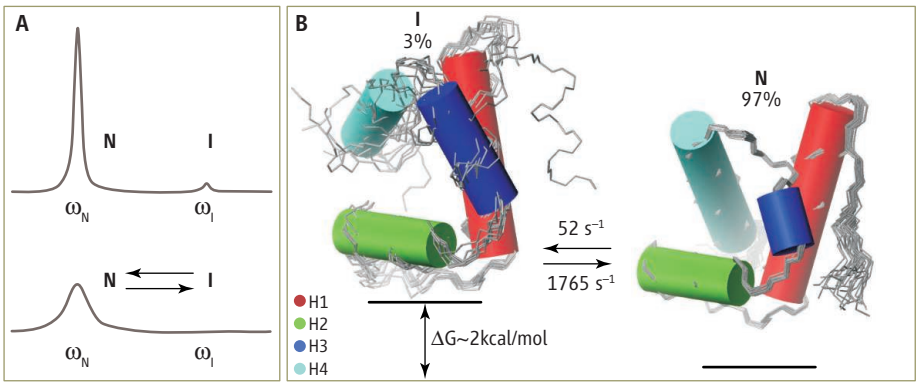

New view. NMR and computational methods provide a high-resolution image for the excited state structure of the FF folding intermediate. (**A**) Dynamic transitions between the ground native (N) and intermediate excited (I) state cause chemical shift line broadening. (**B**) Excited state folding intermediate (I) and ground state native (N) structures of the FF domain. Shown are the fractional populations of the two states along with the corresponding free-energy difference (ΔG) and rates of interconversion at a temperature of 30°C.

chemical shifts have very effectively been used as structural fingerprints that make it possible to infer structural similarities between different proteins or regions within a protein. Indeed, the most compelling link between excited states and protein function have come from finding similarities between their chemical shifts and those observed for different functional forms of the ground state, including those involved in various stages of catalytic cycles (*1*), following phosphorylation (*2*), and upon binding molecular partners (*3*).

The determination of an excited state structure by Korzhnev *et al*. awaited two major advances. First, in a series of recent breakthroughs (*8*, *9*), investigators showed that integrating chemical shift data into structure prediction algorithms provided a route for robust and accurate structure determination of proteins that are up to 120 amino acids in length. Here, a protein is divided into segments, and candidate structures for each segment are obtained by scanning the protein structure database for similar amino acid segments. The segments are then threaded together and energetically refined to predict a protein structure. A major problem has been sampling the native structure from an astronomical number of possibilities. By using chemical shift fingerprinting to narrow down candidate structures, the conformational search is guided early on toward the lowest-energy conformation. Second, recent developments in NMR experimentation and labeling schemes (*7*) have expanded the applicability of experiments with a technique called relaxation dispersion. This has made it possible to access complete sets of backbone chemical shift data for excited states as well as another NMR observable, called residual dipolar couplings (RDCs) (*10*), which probes the orientation of backbone amide vectors in the excited state.

By feeding excited state chemical shifts and RDC data into a structure prediction program called CS-Rosetta (*8*), Korzhnev *et al*. successfully determined the high-resolution structure of a protein in an excited state that has an equilibrium population of just ~3% and a lifetime of merely 1 ms (see the figure). Specifically, they solved the structure of a folding intermediate of the 71-residue FF domain from HYPA/FBP11. Intermediates are short-lived species that form ubiquitously during protein folding and that are thought to act as stepping-stones toward the native ground state. Although researchers have proposed high-resolution structures for protein intermediates (*4*, *11*), these studies relied either on limited data to build qualitative models or on finding conditions that "trap" the intermediate forms.

Korzhnev *et al*. convincingly establish the validity of their excited state structure, which is not an easy task considering its transient high-energy nature. First, the structure is in excellent agreement with the input experimental data, and similar structures are obtained with or without inclusion of the RDCs. Second, the authors made pointed predictions based on their excited state structure, and followed these with experimental tests. In particular, by chopping off the carboxyl-terminal portion of the FF domain, which is structured in the ground state but predicted to be disordered in the excited state, they successfully trapped the excited state, as verified by NMR chemical shift fingerprinting. Finally, the structure is consistent with a large body of data, most notably phi values, which measure the role of individual residues in stabilizing the transition state.

How does the structure of the excited state intermediate differ from that of the ground state, and what does it teach us about the folding pathway? The ground state structure consists of four helices (H1 to H4). Although the orientation and lengths of H1 and H2 and the connecting loop are similar in both states, H3 is longer in the excited state, and includes residues from the H3-H4 loop and the beginning of H4. The nonnative H3 forms several nonnative interactions with H1 and H2 and prevents formation of H4, which is disordered in the excited state. Thus, even though the excited state is destabilized relative to the native ground state by only 2 kcal/mol, or the equivalent of roughly one N-H-O hydrogen bond, the two states have very different secondary and tertiary structures and levels of dynamic disorder. This adds to a growing view that folding intermediates are not simply native structures lacking a subset of interactions; rather, they can have unique structures that are stabilized by nonnative interactions (*11*, *12*). The need to disrupt these nonnative interactions offers an explanation for why the transition toward the native state is rate-limiting during protein folding. It is also conceivable that the structure carries hidden clues about whether the intermediate facilitates FF folding or is merely a by-product of evolutionary pressures that seek to optimize function over folding.

Korzhnev *et al*. usher in a new era in which researchers can determine the high-resolution structure of the excited states of proteins with lifetimes on the order of milliseconds. Other developments involving the joint application of computational approaches and NMR RDC data are making it possible to get a glimpse of transient state structures that have even shorter lifetimes, on the order of nanoseconds to microseconds (*13*–*15*). It seems inevitable that the entire protein structure landscape will soon succumb to NMR and computation.

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Biodiversity Conservation: Challenges Beyond 2010

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The continued growth of human populations and of per capita consumption have resulted in unsustainable exploitation of Earth's biological diversity, exacerbated by climate change, ocean acidification, and other anthropogenic environmental impacts. We argue that effective conservation of biodiversity is essential for human survival and the maintenance of ecosystem processes. Despite some conservation successes (especially at local scales) and increasing public and government interest in living sustainably, biodiversity continues to decline. Moving beyond 2010, successful conservation approaches need to be reinforced and adequately financed. In addition, however, more radical changes are required that recognize biodiversity as a global public good, that integrate biodiversity conservation into policies and decision frameworks for resource production and consumption, and that focus on wider institutional and societal changes to enable more effective implementation of policy.

Biodiversity—the variety of genes, species, and ecosystems that constitute life on Earth—provides numerous essential services to society. These include material goods (for example, food, timber, medicines, and fiber), underpinning functions (flood control, climate regulation, and nutrient cycling), and nonmaterial benefits such as recreation (*1*). Biodiversity can contribute to agriculture through pollination and pest control (*2*), provide carbon storage and sequestration (*1*), and positively affect human physical and mental health (*3*). Biodiversity also secures long-term flows of benefits from nature by providing resilience to disturbance and environmental change (*2*). These and other economic and social contributions are substantial (*4*), with recent estimates claiming that the economic value of benefits from biodiverse natural ecosystems may be 10 to 100 times the cost of maintaining them (*5*).

The imperative to reduce human impacts on biodiversity has wide political recognition. The United Nations Convention on Biological Diversity (CBD), agreed at the 1992 UN Conference on Environment and Development, is one of the most widely ratified treaties in the world. Since 2002, 193 parties to the CBD have committed themselves to substantially reducing rates of biodiversity loss by 2010; this goal was later endorsed by the World Summit on Sustainable Development and incorporated into the UN Millennium Development Goals in 2005 (*6*). There is an increasing array of national, regional, and international policy mechanisms aimed at biodiversity conservation; for example, 87% of the signatories to the CBD have now developed National Biodiversity Strategies and Action Plans, and thus have frameworks for tackling biodiversity loss at national scales (*7*).

Millions of people worldwide actively support biodiversity conservation. The Nature Conservancy in the United States and the Royal Society for the Protection of Birds in the United Kingdom have a combined membership exceeding 2 million, and the World Wide Fund for Nature (WWF) network has more than 5 million supporters worldwide. In developing countries, membership of conservation organizations is much smaller than in wealthy nations but is often influential and growing rapidly (*8*). Of course, support extends well beyond this to a growing range of local, national, and regional civil society organizations and community groups that are involved in activities related to biodiversity, in some cases building on indigenous knowledge of its management (*9*). Conservation biology has become a recognized academic discipline, with its own journals and postgraduate courses, although most of this capacity remains concentrated in the developed world (*10*) despite recent growth in developing-world professional training programs (*11*).

Yet biodiversity continues to decline, even though worldwide conservation efforts are increasing (*1*, *7*, *12*). In this article we review the scope and achievements of these efforts, and outline the key challenges that we believe must be

Fig. 1. Community tree nursery in Harapan Forest, lowland Sumatra, Indonesia, where an innovative 2007 law enabled management of logging concessions for ecosystem restoration rather than timber extraction. Harapan's is the first such license, and the concession now covers nearly 100,000 ha of biodiversity-rich habitat (**inset**) with restoration being carried out under a joint project of Burung Indonesia, the Royal Society for the Protection of Birds (UK), and BirdLife International. The Indonesian government is committed to expanding the area licensed for forest restoration to 2 million ha by 2020. [Photo: Harapan Rainforest Initiative/M. Lambertini]

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met for conservation to succeed post-2010. We draw on a broad range of individual perspectives across the natural and social sciences, as researchers and practitioners from both developed and developing countries.

Conservation Approaches

Conservation paradigms, practices, and policies have shifted over time and have been variably successful (*13*). In recent decades, traditional approaches to conservation—such as the creation of national parks—have evolved to encompass awareness of the diverse benefits provided by protected areas, the importance of local conservation initiatives and interests in protected area management, and the need to address the opportunity costs of conservation among the rural poor. Ecological restoration, both within and outside protected areas, is being increasingly applied worldwide (*14*). Actions for species, such as targeted habitat management, removal of invasives, captive breeding, and reintroduction, have yielded notable successes; among many examples, at least 16 bird species extinctions have been prevented by such means between 1994 and 2004 (*15*).

Since 1992, the global network of protected areas has continued to grow steadily, increasing yearly by an average 2.5% in total area and 1.4% in numbers of sites, and by 2006 covering more than 24 million km^2 in about 133,000 designated sites (*7*). Despite some failings, protected areas overall remain a core element of biodiversity conservation (*16*, *17*).

Fig. 2. A flower collector in Flower Valley, South Africa, harvesting pincushions (*Leucospermum* spp.) as part of a sustainable use initiative. Sales of sustainably harvested wild fynbos flower bouquets help to subsidize the conservation costs of the site. [Photo: Juan Pablo Moreiras/Fauna & Flora International]

Landscape-scale approaches to reducing biodiversity loss have become increasingly important, especially in wealthier countries (*18*). These include trans-boundary conservation [e.g., the Great Limpopo Transfrontier Park (*19*)], payments for environmentally sensitive farming (*20*) [such as under the Farm Bill in the United States (*21*) or in the Agulhas National Park in South Africa (*22*)], and large-scale habitat creation and restoration, as seen, for example, in the Oostvaardersplassen project in the Netherlands (*23*) and the Harapan Forest in Indonesia (Fig. 1). These initiatives reflect scientific research showing the importance of maintaining suitably managed habitats, which should be large (*24*) and connected rather than isolated (*25*), within a hospitable matrix (*24*).

Many other approaches to biodiversity conservation have been developed, especially those linked to economic benefits, including sustainable consumptive use (*26*) (Fig. 2) and nonconsumptive uses such as ecotourism (*27*). Some of these help meet the opportunity costs of conservation, which would otherwise preclude conservation choices among poor rural communities. Mechanisms that provide revenue streams from biodiversity through direct payments for conservation (*28*) or payments for ecosystems services (*29*)—for example, through REDD+ schemes (*30*)—are as yet largely experimental in implementation but have potential for considerable impact. (REDD+ is a mechanism for reducing emissions from deforestation, forest degradation and other activities affecting forest carbon stocks.)

Pressures on Biodiversity

Despite these efforts, biodiversity loss is not slowing down. Recent assessment shows a continued, steady overall decline in wild species' population sizes and in the extent, condition, and connectivity of many habitats, with accelerating levels of extinction risk and accelerating or steady declines in the benefits people derive from biodiversity (*7*) (Fig. 3). Although species extinctions are the most conspicuous result of biodiversity loss, it is estimated that distinct subpopulations are becoming extinct some three orders of magnitude faster than species (*31*).

Pressures on biodiversity continue to increase. The key pressures driving biodiversity loss are overexploitation of species, invasive alien species, pollution, climate change, and especially the degradation, fragmentation, and destruction of habitats (*7*). Agriculture is an expanding land use in about 70% of countries (*32*), generally at the expense of biodiversity. Much of the global timber trade is based on unsustainable or illegal logging that destroys biodiversity-rich habitat, as shown across five major timber-producing countries in 2009 where, on average, only 14% of licensed logging area was sustainability-certified, while up to half of all harvesting was illegal (*33*).

Over-abstraction of water for agriculture, industry, and domestic demands contributes to shifts in agricultural patterns; this imposes greater pressure on biodiversity in other locations, as does soil salinization resulting from irrigation in arid regions (*34*). Increasing demand for vegetable oils—for food, cosmetics, and biofuels—has put further pressure on biodiversity; oil palm plantations, for example, cover 13 million ha of the humid tropics, and global demand (largely driven by rising consumption levels in developed and emerging economies) is pushing up prices and incentivizing further expansion (*35*). Remaining terrestrial biodiversity is therefore increasingly confined to fragmented patches separated by expanding cultivation, infrastructure, and residential and industrial development. Marine biodiversity is also under increasing pressure. Steep declines in fish populations and loss of marine habitats have resulted from overexploitation of marine protein, focused on fish at the top of the food chain; increases in poorly managed aquaculture; and direct habitat destruction from coastal development, extractive industries, and pollution (*36*).

Biodiversity also faces new pressures and novel threats (*12*). Further anthropogenic climate change and rising human resource demands will pose immense interlinked challenges. Climate change may force species to shift their ranges (*37*) and disrupts ecological communities (*38*, *39*). Lack of continuous semi-natural habitat or networks of connected habitat patches can restrict the capacity of species to adjust to changing conditions (*40*). Enhanced levels of atmospheric CO_2 also threaten corals through ocean acidification (*41*). New initiatives and technologies aimed at mitigating climate change may have negative effects on biodiversity. For example, technological developments in biofuel production from cellulose could drive the planting of high-yielding perennial C4 grasses, such as *Miscanthus*, on millions of hectares of temperate-zone land not currently used for agricultural production (*42*). Increasing demands for food production resulting from human population growth and dietary shifts require intelligent and integrated solutions, and severe impacts on biodiversity could occur in the absence of such solutions (*43*). On top of these reasonably well-known threats are others that are less well understood, including possible threats from microplastic pollution, nanosilver, biochar, and artificial life (*44*).

Filling Knowledge and Capacity Gaps

Although we now have a great deal of information on the state of biodiversity, the biological and social processes that affect it, and the pres-

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sures and underlying drivers that result in its continued decline (*1*, *7*, *12*), there are also some key knowledge gaps. There are few data on the status, trends, or functional importance of microbes, invertebrates, and many plant groups, or of wild genetic diversity (*45*). Even relatively well-known groups, such as vertebrates, are far better documented in temperate regions than in the much more diverse tropics (*46*). How different components of biodiversity contribute and relate to the provision of services (*47*, *48*) (Fig. 4) or create resilience to environmental change (*49*) is poorly understood. Our knowledge of ecosystem management and restoration is inadequate to meet the challenges of reconciling increased production with sustaining ecosystem services, or of ameliorating the negative effects of climate change. Existing knowledge, often including extensive traditional knowledge (*9*), is generally underused in decision-making at local, national, and international levels. There is an urgent need both to learn from practical experience and to disseminate research findings to practitioners (*50*). Horizon scanning—the systematic search for potential threats and opportunities that are currently poorly recognized—needs to be expanded to identify the currently "unknown unknowns" (*51*).

Moreover, scientific capacity is not equally shared across the globe, and in particular is concentrated in rich developed countries rather than in the regions that face the most substantial challenges to maintaining and enhancing biodiversity. The proposed establishment of an Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services may help to close knowledge gaps and link science and economics to the policy step-change needed to conserve biodiversity (*52*). To be effective, though, it must empower developing country institutions and knowledge-to-policy mechanisms, a process requiring sustained investment and support, combined with enhanced linkages and experience sharing among developing countries.

Scaling Up Success

Conservation interventions that are deemed effective, and the conditions under which they work, need to be identified more consistently, and these successes need to be replicated and scaled up in intelligent and evidence-based ways (*50*). For example, protected areas can be an effective tool for conserving biodiversity, but current networks have considerable gaps; some 20% of 3896 threatened vertebrates are not included in any protected area (*53*), and many protected areas are under-resourced (*54*) or weakly managed (*55*). Although 12% of Earth's land surface has protected-area status, only 0.5% of oceans and 5.9% of territorial seas have been so designated, and more than two-thirds of critical sites for biodiversity have incomplete protection or none at all (*7*). New protected areas can draw on a broad range of possible governance models, including community and indigenous conserved area approaches, to fit their particular circumstances (*56*, *57*). Protected areas need to be managed as a coherent network rather than as isolated habitat islands in order to sustain biodiversity, particularly in the face of climate change (*39*). The challenges of working across administrative and national boundaries are considerable, but experience suggests they are not insurmountable (*58*).

Scaling up successful approaches requires much greater investment in biodiversity conservation, by at least an order of magnitude (*59*, *60*). National investment is poorly documented but is increasing (and diversifying) in at least some biodiversity-rich countries, such as Mexico (*61*). International financial investment in biodiversity conservation has been slowly increasing (*7*) and is estimated to have grown around 38% in real terms between 1992 (when the CBD came into force) and 2006 (*62*). The sums involved are still tiny relative to the amounts spent on environmentally damaging subsidies (*63*). They need to be enormously scaled up (*59*) to benefit those countries that hold the richest biodiversity (*64*).

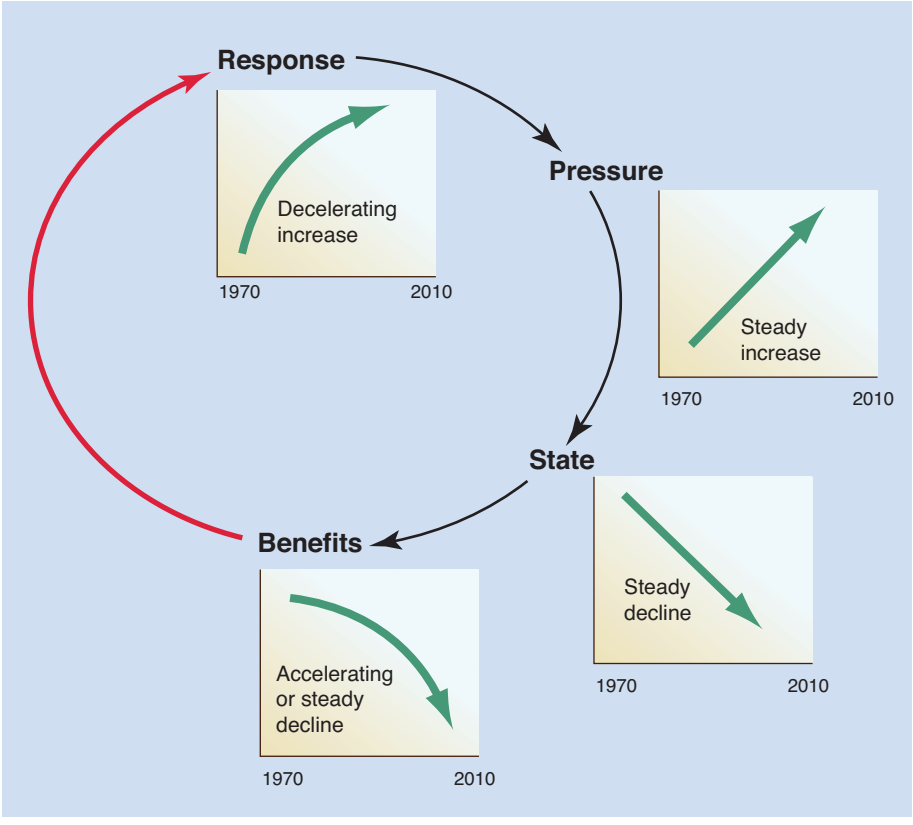

Fig. 3. The feedback loop between responses to biodiversity loss, the pressures on biodiversity, the state of biodiversity, and the benefits it provides. The arrow linking benefits to responses is highlighted because of its particular importance: Responses are put in place in relation to how far the maintenance of biodiversity is valued as a benefit to society and individuals. Thumbnail graphs show the overall trend in each of these aspects over the past 4 decades [simplified from (*7*)]. Although responses continue to grow, the rate of increase is slowing and not keeping pace with the steady rise in pressures. A corresponding steady decline in state is linked to a steady or possibly accelerating decline in benefits.

Fundamental Challenges Beyond 2010

Filling gaps in our knowledge and building on success, through scaling up and further investment in conservation that works, are critical if we are to gain some breathing space for biodiversity but will not suffice to achieve its maintenance long-term. This year the global community has an opportunity to go much further. The UN has declared 2010 the International Year of Biodiversity and has agreed to hold a special session of this year's General Assembly devoted to biodiversity, partly in the context of reviewing progress in achieving the Millennium Development Goals. At the 10th Conference of the Parties of the CBD (Nagoya, Japan, October 2010), governments will not only assess whether they met the 2010 biodiversity target, but are expected to adopt a new strategic plan containing a vision for 2050 and new biodiversity targets to be achieved by 2020.

To address the continued global loss of biodiversity, we propose the pursuit of three interconnecting priorities: (i) to manage biodiversity as a public good, (ii) to integrate biodiversity into public and private decision-making, and (iii) to create enabling conditions for policy implementation.

Managing biodiversity as a public good. An appreciation of biodiversity as a public good (*65*) and of its economic value (*66*) is, we believe,

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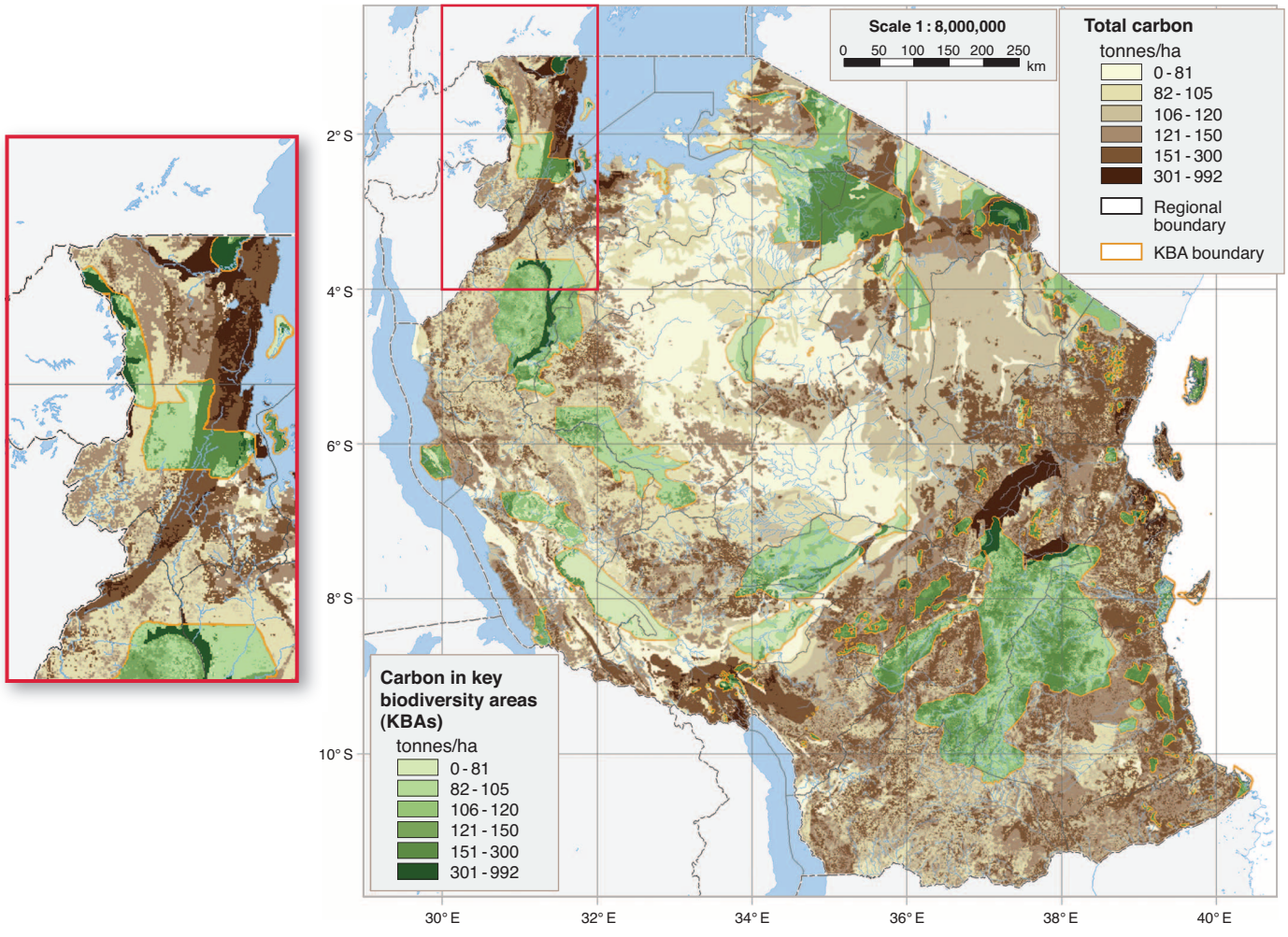

Fig. 4. Key biodiversity areas and carbon density (in biomass and soil) in Tanzania [from (*48*)]. Integrating data on terrestrial carbon with areas important to biodiversity conservation can help decision-makers to take account of multiple benefits and trade-offs when developing REDD+ schemes, a promising example of payments for ecosystem services.

central to future effective conservation. Biodiversity loss is rarely the intended consequence of human actions; more often it is an unintended side effect of decisions taken for other reasons—an economic "externality" (*67*). Biodiversity is a special kind of externality, as the impacts of a particular action are often distant in space and time (e.g., local rainforest loss may affect the global carbon cycle, with consequences for future generations). This makes effective regulation difficult, as no single body has jurisdiction over the world's biodiversity. It also makes transaction-based solutions difficult, because those who damage biodiversity are often widely separated, in space or time, from those who experience the consequences. Actors have few incentives or opportunities to change their behavior, whether they are smallholder households planning their annual agricultural cycles or large multinational companies determining their corporate priorities. Thus, understanding and managing biodiversity as a global public good, which must be provided through conscious collective choices (*68*), is fundamental to achieving its conservation (*5*).

The recognition of biodiversity as a public good is not a new concept, and in recent years economists have made substantial progress in developing valuation techniques that quantify the local and global benefits of biodiversity (*69*). Measuring the economic values of biodiversity (*5*) and estimating spatially explicit economic values of services across landscapes to inform management decisions (*70*) are vital. However, making these values explicit is insufficient to bring about a change in behavior, unless supporting public policies are in place that either reward positive individual actions or penalize harm. Economists need to work more closely with conservationists and policy makers to develop intervention strategies that shift individual actors toward more biodiversity-friendly behavior, using regulatory devices as well as incentives, thereby securing the provision of biodiversity conservation as a global public good.

Integrating biodiversity into public and private decision-making. The value of biodiversity must be made an integral element of social, economic, and political decision-making, as is starting to happen with carbon and climate change. Government, businesses, and civil society all have crucial roles in this transition.

For government, maintenance of stocks of natural capital must become an explicit, accountable, and implemented element of policy. Concern for biodiversity cannot be restricted to a nation's environment ministry but must extend across all sectors of government, such as treasury, industry, and defense. Policy change will require clear and cost-effective metrics of natural capital consumption and depletion (*71*) and the development of systems of public accounts that include both sustainability (*72*) and the specific issue of biodiversity loss (*5*). Government staff and politicians may need in-service training in biodiversity science and ecological economics, with effective research support. Research investment will need to focus on applied transdisciplinary problems. Government will need to remove perverse subsidies detrimental to biodiversity, such as in agriculture, forestry, and fisheries. Fishing subsidies encourage overexploitation of two-thirds of fish stocks across the globe, threat-

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ening both the fishing industry (worth $80 billion to $100 billion per year) and the 27 million people dependent on it (*5*, *73*). Government policy needs to integrate biodiversity conservation, poverty alleviation, and the demands of a sustainable economy (*74*) to meet the Millennium Development Goals (*75*).

The actions of the private sector are central to the future of biodiversity, as the CBD recognized in the context of the 2010 biodiversity target. Corporate environmental performance is increasingly important to investors and therefore corporate leaders (*76*), and many initiatives now exist to address corporate biodiversity impacts in particular business sectors or individual corporations (e.g., in minerals extraction). Yet a recent survey found that only two of the Financial Times Stock Exchange (FTSE) 100 companies recognize biodiversity to be of strategic importance to their business (*5*). Biodiversity lacks the visibility achieved by energy and climate change as issues important to corporate decision makers (*77*). Consistent government regulation is important in providing a level playing field for corporate environmental innovation and competition, but there are challenges in extending regulation internationally (*78*).

Civil society organizations have an important role in building tri-sector partnerships with government and business to promote effective action to conserve biodiversity, and in encouraging their supporters as citizens and consumers to demand reform by the government and business. Consumer initiatives such as certification schemes that seek to influence how products are produced across global supply chains (e.g., the Forest Stewardship Council, Marine Stewardship Council, Fair Trade) have a symbolic and educational value, but the real challenge is to transform production and consumption into sustainable patterns so that such arrangements are the norm and not the exception (*79*). Public education about biodiversity must extend beyond the ecology of near-extinction to explain the links between biodiversity loss and consumption choices. Debates about these links are particularly urgent in emerging markets in countries with rapid economic growth, especially India and China.

Creating enabling conditions for policy implementation. Good decision making at all levels is necessary but insufficient to achieve biodiversity conservation. We believe that policy responses to biodiversity loss generally fail to include a vital step: the establishment of appropriate institutions, governance, and behaviors.

Potential responses to environmental degradation can be placed into three broad tiers (Table 1) (*80*). Existing efforts to address biodiversity loss have tended to jump from tier 1, the generation of knowledge, to tier 3, the design of appropriate instruments (such as national legislation or international treaties), without ensuring that the enabling conditions are in place.

For example, in the case of direct payments for conservation in developing countries, a sound knowledge base demonstrates how biodiversity can be damaged when it is treated as an open-access resource not managed by common-property institutions, and one proposed response aims to pay resource users directly to achieve conservation goals (*28*). However, the critical, but often missing, middle tier is the existence of institutions and governance for designing and implementing payments, together with the associated monitoring and regulation (*81*).

Although REDD+ is not specifically designed to address biodiversity conservation, it has the potential to provide such co-benefits and it illustrates the lack of attention to middle-tier strategies in contemporary environmental policy. With REDD+, a sound knowledge base shows the impacts of forest loss on global carbon emissions. A proposed response aims to use markets and incentives to pay resource users in order to alter their current patterns of land management to stem the loss of forest cover. However, the critical middle tier that has been underemphasized is the need for appropriate institutions and governance that would permit the efficient operation of markets for forest carbon (*82*). Markets cannot work without clear property rights and enforceable contracts. Having decided that a market for forest carbon is an appropriate instrument for delivering desired outcomes, a range of countries are making considerable efforts and investment to develop relevant institutions and governance structures, but it is far from clear that the regions that have the most potential from a forest carbon perspective are also the ones where conducive institutions and governance structures exist or can be created.

Table 1. The three different tiers within which responses to biodiversity loss are typically located. Each tier is equally important, but experience suggests that the crucial element that is missing from many current initiatives is the middle tier. It is important to ensure that appropriate institutions and governance structures exist to enable the effective use of targeted instrumental interventions to address biodiversity loss. [Adapted from (*80*)]

Tier 1: Foundational	• Knowledge about social and biological dimensions of biological loss
Tier 2: Enabling	• Institutions/ governance • Social/behavioral patterns
Tier 3: Instrumental	• Legislation • Markets/incentives • Technology

Conservation appears to succeed best where an adequate knowledge base is combined with appropriate institutional structures and patterns of societal behavior that enable the adoption of targeted instruments. Globally, and unsurprisingly, current conservation success is strongly linked to good governance (*83*). This is evident in the many examples of effective communal management (*84*, *85*) as well as in "traditional" national parks such as Yellowstone in the United States, which was created at a time of rapid state-sponsored scientific exploration and strong federal governance (*86*).

There are often good reasons for failure to address the enabling factors for appropriate action. Institutions and governance are not easy to change, especially if there are deeply entrenched cultures of patronage and corruption that govern the use and management of natural resources; moreover, governance mechanisms at different levels (local, regional, and national) may differ or even be contradictory (*87*). Conservationists may not feel that it is appropriate to address wider political problems and may be poorly equipped to do so. However, creating enabling conditions for conservation is an essential component of the solution, requiring conservationists to join with wider civil society groups pressing for governance reform and institutional change. Achieving political recognition of the economic value of biodiversity and its role in underpinning human development and welfare is an important element of this approach. As the obviously artificial but symbolically important 2010 milestone is passed, this imperative can only grow stronger. Within this bigger picture, a key element involves "reconnecting" people—the growing majority who now live in urban areas and lack daily contact with farms or forests—to nature (*88*). Alongside this, there is a need for a better understanding of the ways in which such a reconnection can be translated into the mobilization of the political constituencies that are necessary to create resilient conservation institutions (*89*).

Outlook

The challenges of addressing the social and behavioral contexts for biodiversity conservation are daunting. We are far from including biodiversity in our conventional measures of well-being, which focus on wealth creation and internationally recognized estimates of GDP (*90*). Although there have been attempts to redefine these (including, for instance, the Human Development Index and green national accounts), the mainstream view of well-being and of national development remains focused on narrowly defined economic growth (*68*). Furthermore, the current recession only strengthens the emphasis on growth. The transition to sustainability will not be easy, but it is central to securing a future for biodiversity (*91*). Conservation strategies, in concert with other environmental policies, must address seemingly intractable and politically unpalatable issues. In both developed and emerging economies, we need to reduce the carbon and material throughput demanded by current patterns of production and consumption if we are to create viable and democratically acceptable trajectories of contraction and convergence in resource use. In parallel, we must recognize that successful human

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development agendas are underpinned by functional ecosystems, and by biodiversity. This is the year in which governments, business, and civil society could decide to take seriously the central role of biodiversity in human well-being and quality of life (*92*) and to invest in securing the sustainable flow of nature's public goods for present and future generations.

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Detection of a Trailing (L5) Neptune Trojan

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The dynamics of objects in relatively stable reservoirs such as the main asteroid belt, Kuiper Belt, and Lagrangian regions of Jupiter and Neptune (the Trojans) have a fossilized imprint from the evolution of the solar system. Trojans lead (L4) or trail (L5) a planet by ~60° near the two triangular Lagrangian points of gravitational stability. Trojans share their planet's orbital period and semimajor axis and thus are extremely sensitive to the formation and migration of their planet (*1*–*3*). Coarse or irregular planetary migration, for example, results in the depletion of the associated Trojan reservoir (*1*, *4*–*7*). The first Neptune Trojan was discovered near the L4 region in 2001, and several more L4 Neptune Trojans have been discovered in recent years (*3*). Jupiter has almost 3000 known Trojans, but the other giant planets, Saturn and Uranus, are not expected to have substantial numbers because their Lagrangian regions are more dynamically unstable (*5*, *7*, *8*). We used the Subaru 8.2-m and Magellan 6.5-m telescopes to obtain an ultradeep survey (reaching apparent red magnitudes as faint as m_R = 25.7) of the Neptune L5 and L4 Trojan regions.

The Neptune Trojans are not just 60° from the planet but may librate up to 30° from the Lagrangian points over a 10,000-year time scale (*2*). Thus, the Neptune Trojan regions cover thousands of square degrees on the sky. At the Neptune L5 region, it is extremely difficult to detect objects because the line of sight is near the galactic center. This creates major confusion with background stars. In order to determine whether L5 Neptune Trojans exist, we devised a special observing strategy. We used images from the UK Schmidt Telescope of the digitized sky survey to locate regions where dust clouds obscure the light from stars in the galactic plane. We found tens of square degrees where this occurred near Neptune's orbital plane and in the L5 Trojan region. In addition, some fields were along the New Horizons flight path to Pluto and beyond, allowing detection of objects the spacecraft could image.

We found an L5 Neptune Trojan (2008 LC18) with Subaru on UT 7 June 2008 (Fig. 1A). By placing artificial objects in our L4 and L5 Neptune Trojan fields, we estimated that the higher stellar background of the L5 fields lowered our detection efficiency by about 55% (Fig. 1B). The one L5 Trojan found in 19 square degrees gives a rough estimate of the L5 population. By assuming the L5 cloud covers 1500 square degrees (±15° in ecliptic longitude and ±25° in ecliptic latitude from the L5 point), we estimated that there are 150^{+200}_{-100} Neptune Trojans in the L5 cloud brighter than 24th magnitude (radii > 40 km). This, within uncertainties, matches the number of estimated Neptune Trojans of this brightness in the L4 cloud, 250 ± 100, where we have combined a previous survey (*3*) with additional L4 observations from us in 2007–2009 (a total of five Neptune Trojans were detected in 30 square degrees in the L4 region). These results are consistent with similar populations in the L4 and L5 clouds. This similar symmetry suggests there was no gas drag during capture (*9*). The large inclination for the L5 Neptune Trojan 2008 LC18 ($i \approx 28°$) is similar to those of some of the L4 Neptune Trojans, indicating a common capture mechanism for both regions. The large inclinations of many of the Neptune Trojans suggest that captures occurred during either a slow, smooth planetary migration process (*7*, *10*, *11*) or after any substantial planetary migration through a freeze-in circularization process (*1*, *3*, *12*). The expected large number of high-inclination Neptune Trojans means that capture occurred with a dynamically excited planetesimal population.

A

Name	L	*a* (AU)	*i* (°)	*e*	*m* (mag)	*r* (km)
2001 QR322	L4	30.37	1.3	0.03	22.5	70
2004 UP10	L4	30.28	1.4	0.03	23.3	50
2005 TN53	L4	30.24	25.0	0.07	23.7	40
2005 TO74	L4	30.25	5.2	0.05	23.2	50
2006 RJ103	L4	30.15	8.2	0.03	22.0	90
2007 VL305	L4	30.12	28.1	0.07	22.2	80
2008 LC18	L5	30.01	27.5	0.08	23.2	50

B

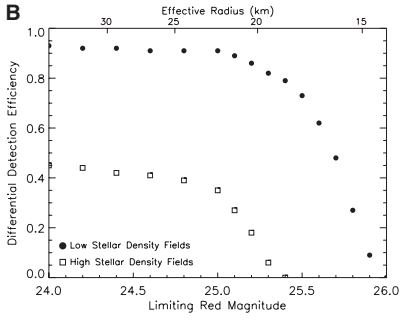

Fig. 1. (**A**) The known Neptune Trojans. The Neptune Trojans with the highest inclinations have the largest eccentricities. The heliocentric ecliptic osculating orbital elements are from the Minor Planet Center and are the semimajor axis (*a*), inclination (*i*), and eccentricity (*e*). All known Neptune Trojans were observed over more than 1 year. Numerical integration of their orbits using the Mercury program shows that the orbits are stable for the age of the solar system. The radii (*r*) of the Neptune Trojans were determined by assuming an albedo of 0.05 and using the equation $r = [2.25x10^{16}\ R^2\Delta^2/p_R\phi(0)]^{1/2}\ 10^{0.2(m_\odot - m_R)}$, where *R* is the heliocentric distance in astronomical units (AU), Δ is the geocentric distance in AU, $m_\odot$ is the apparent red magnitude of the Sun (–27.1), p_R is the red geometric albedo, m_R is the apparent red magnitude of the Trojans, and $\phi(0)$ = 1 is the phase function at opposition. (**B**) Detection efficiency of the survey fields versus the apparent red magnitude. The efficiency was determined by placing artificial objects with known magnitudes matched to the point-spread function of the images with motions expected of a Neptune Trojan (about 4 arc sec per hour). Effective radii were calculated assuming an albedo of 0.05 (*13*). Three images separated by about 1 hour each were imaged for each field in order to detect moving solar system objects. This survey was conducted in a similar manner as our previous ultradeep surveys for planetary satellites (*14*, *15*).

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Pulsar Discovery by Global Volunteer Computing

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Einstein@Home (*1*) (E@H) is a volunteer distributed computing project (*2*). Members of the public sign up their home or office computers (hosts), which automatically download work units from the servers, carry out analyses when idle, and return results. These are automatically validated by comparison with results for the same work unit produced by a different volunteer's host. More than 250,000 individuals from 192 countries have contributed; each week about 100,000 different computers download work. The aggregate computational power (0.25 Pflop/s) is on par with the largest supercomputers. E@H's primary goal is to detect gravitational waves from rapidly spinning neutron stars in data from Laser Interferometer Gravitational-Wave Observatory (LIGO) and VIRGO (*1*).

Since 2009, about 35% of E@H compute cycles have also been used to search for pulsars in radio data from the Pulsar ALFA (PALFA) project [supporting online material (SOM)] at the 305-m Arecibo Telescope (Puerto Rico). Data disks are sent to Cornell University's Center for Advanced Computing (United States), where data are archived. For E@H, data are transferred to Liebniz Universität (Hannover, Germany), dedispersed for 628 different dispersion measures (DM ∈ [0, 1002.4] pc cm^{-3}), and resampled at 128 μs. Hosts receive work units containing time series for four DM values for one beam. Each is 2 MB in size, covering 268.435456 s. A host demodulates each time series (in the time domain) for 6661 different circular orbital templates with periods greater than 11 min (our Galaxy has even shorter period binaries). The grid of templates is spaced so that, for pulsar spin frequencies below 400 Hz, less than 20% of signal-to-noise ratio is lost. Fourier algorithms sum up to 16 harmonics. A total of 1.85% of the power spectrum is removed to eliminate well-known sources of radio frequency interference. A significance ($S = -\log_{10} p$, with p the false-alarm probability in Gaussian noise) is calculated at each grid point. After ~2 central processing unit hours, the host uploads the 100 most significant candidates to the server.

When all work units for a given beam are complete, the results are postprocessed on servers at Hannover. Candidates with $S > 15$ are identified by eye, then optimized with PRESTO (www.cv.nrao.edu/~sransom/presto/) (SOM). To date E@H has searched 27,000 of 68,000 observed beams. It has redetected 120 pulsars, most in the past 4 months, because code and algorithm optimizations sped up the search by a factor of ~7.

On 11 July, the 24-ms PSR J2007+2722 was discovered with a significance of $S = 169.7$ (Fig. 1) in survey data from February 2007. It was later re-detected in another PALFA survey observation. Follow-up observations were done by the Green Bank Telescope (GBT, United States), the Lovell Telescope at Jodrell Bank Observatory (United Kingdom), the radio telescope at Effelsberg (Germany), the Westerbork Synthesis Radio Telescope (WSRT, Netherlands), and Arecibo. The period-averaged flux density is 2.1 mJy (1 Jy = 10^{-26} W m^{-2} Hz^{-1}) at 1.5 GHz. Gridding observations using Arecibo and WSRT unambiguously associate the pulsar with a source in an archival Very Large Array (VLA) C-array observation, having 1.2 mJy flux density at 4.86 GHz, at right ascension (RA) 20^{h}07^{m}15^{s}.77 and declination (Dec) 27°22′47″.7 (J2000) with uncertainty $\lesssim 1''$. The pulsar is not in a supernova remnant or globular cluster and has no counterpart in x-ray or gamma-ray point-source catalogs. The DM of 127 pc cm^{-3} implies a distance of 5.3 kpc (*3*). The full pulse width between the outer half-maxima is $W \approx 224°$. The wide pulse and initial polarization observations indicate that the pulsar likely has nearly aligned magnetic and spin axes.

The pulsar's barycentric spin frequency (*4*) is 40.820677620(6) Hz at MJD 55399.0. With the VLA position, the 2010 data give limits $|\dot{f}| < 3 \times 10^{-14}$ s^{-2}, magnetic field $B < 2.1 \times 10^{10}$ G, and spin-down age $> 21 \times 10^{6}$ years. These limits and lack of a companion mean that J2007+2722 is likely the fastest-spinning disrupted recycled pulsar yet found (*5*). However we cannot rule out it having been born with low B (*6*). Either way, PSR J2007+2722 is a rare, isolated low-B pulsar, which contributes to our understanding of pulsar evolution.

This result demonstrates the capability of "consumer" computational power for realizing discoveries in astronomy and other data-driven science.

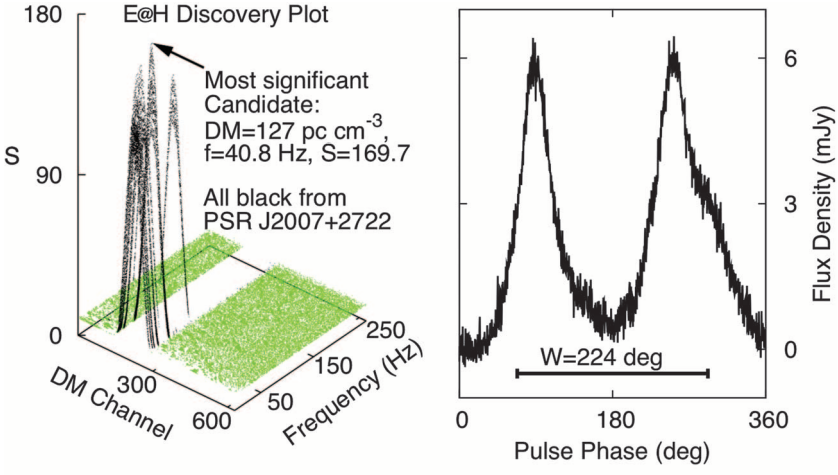

Fig. 1. (**Left**) Significance S as a function of DM and spin frequency (all E@H results for the discovery beam). (**Right**) The pulse profile at 1.5 GHz (GBT). The bar illustrates the extent of the pulse.

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7. We thank Einstein@Home volunteers, who made this discovery possible. The computers of C. and H. Colvin (Ames, Iowa, USA) and D. Gebhardt (Universität Mainz, Musikinformatik,Germany) identified J2007+2722 with the highest significance. This work was supported by Canada Foundation for Innovation, Canadian Institute for Advanced Research, fonds québécois de la recherche sur la nature et les technologies, Max Planck Gesellschaft, National Astronomy and Ionosphere Center, National Radio Astronomy Observatory, Natural Sciences and Engineering Research Council (of Canada), NSF, and Netherlands Organization for Scientific Research, Science and Technology Facilities Council; see the SOM for details.

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Oscillating Gene Expression Determines Competence for Periodic *Arabidopsis* Root Branching

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Plants and animals produce modular developmental units in a periodic fashion. In plants, lateral roots form as repeating units along the root primary axis; however, the developmental mechanism regulating this process is unknown. We found that cyclic expression pulses of a reporter gene mark the position of future lateral roots by establishing prebranch sites and that prebranch site production and root bending are periodic. Microarray and promoter-luciferase studies revealed two sets of genes oscillating in opposite phases at the root tip. Genetic studies show that some oscillating transcriptional regulators are required for periodicity in one or both developmental processes. This molecular mechanism has characteristics that resemble molecular clock–driven activities in animal species.

Formation of periodic modular structures is a common developmental feature in both animals and plants (*1*, *2*). The body axis of many metazoans—including species of arthropods, annelids, and vertebrates—is organized into segments. This organization is established during embryogenesis by successive addition of segments to an elongating posterior body region (*3*). In plants, branching of shoots and roots during postembryonic development produces repeating units (phytomers and lateral roots, respectively) along the growing longitudinal axis. Leaves are generated in a regular phyllotactic pattern, and lateral roots (LRs) are continuously produced from the primary root (Fig. 1A) as it grows, following the gravity vector (*4*).

In vertebrates, segmentation is coordinated by a molecular clock that converts temporal information into a periodic spatial pattern, which precisely positions somites along the anterior-posterior axis (*3*, *5*). In the plant shoot apical meristem, there is evidence that differential hormone distribution may be involved in positioning leaf primordia (*6*). In the root, the developmental mechanism by which newly formed organs are positioned in time and space along the primary root remains largely uncharacterized. LR formation begins when selected pericycle cells become LR founder cells. However, the process underlying the selection of these cells is unknown. After specification, LR founder cells undergo a stereotypic patterning to form a LR primordium (*7*). Eventually, the newly formed primordia develop into LRs that emerge through the primary root tissues. Emergence is highly dependent on environmental conditions (*8*). An auxin-based oscillatory mechanism has been hypothesized to be operating to initiate LR primordia in roots (*9*). Our evidence suggests that LR positioning is instead mediated by oscillating genes that establish the temporal and spatial distribution of LRs along the primary root axis.

Periodic branching and bending require an endogenous mechanism. Enhanced transcriptional response to auxin in the basal meristem, as reported by the DR5:GUS synthetic promoter construct, has been proposed to be involved in formation of LR primordia (*10*). To investigate this hypothesis in vivo and in real time, we fused the DR5 promoter to the Luciferase coding region to conduct nondestructive reporter assays (*11*). We observed that DR5:Luciferase expression rhythmically pulsed with a period of ~6 hours in the basal meristem and the elongation zone (Fig. 1, B and C, and movies S1 and S2). We designated this whole region as the oscillation zone (OZ). Examination of gene expression relative to the root's developmental zones is relevant because, in the *Arabidopsis* root, cells at a fixed spatial position change their status over time. In addition, we observed that the pulses of DR5 expression preceded the establishment of static points of DR5:Luciferase expression, which we termed prebranch sites. Prebranch sites can subsequently develop into new LRs (Fig. 1D and fig. S1). Prebranch sites from which LRs did not emerge were examined microscopically, and early-stage LR primordia (*7*) were found in all cases. Thus, prebranch site formation predicts the spatial position of LRs in the primary root, and we hypothesize that the oscillation reported by DR5 results in competence to form LRs at the prebranch sites.

It has been previously described that distance or cell number between consecutive LRs or LR primordia was variable (*12*); we therefore investigated whether LR positioning might follow a temporal distribution. We measured the time between adjacent prebranch sites and tested the distribution of the cumulative function for normality. We found that the frequency of prebranch site production followed a normal distribution (*P*-value = 1.8*e*-06 in an Anderson-Darling normality test) with a mean period of ~6 hours (Fig. 1E). In addition, because previous reports had shown a correlation between the bends formed by the primary root while it grows and LR formation, we also measured the time between consecutive bends (Fig. 1F). Remarkably, we found that the frequency of bending also followed a normal distribution ($P = 0.017$ in an Anderson-Darling normality test) with a mean period similar to that of prebranch site initiation. We observed that the DR5 oscillation seems to occur prior to changes in growth direction of the primary root (Fig. 1C). This suggests that bending may also be a consequence of a developmental mechanism reported by DR5, although additional regulation by external cues, such as gravity, cannot be excluded.

A characteristic of endogenous mechanisms that track time in living organisms is their capacity to compensate for changes in temperature, which buffers the periodic processes against variations due to external conditions (*13*, *14*). To determine if this is the case for prebranch site formation, we grew plants at different temperatures and observed the number of prebranch sites formed during 6 days of growth. We found that the number of prebranch sites remained largely unchanged in plants grown between 18° and 24°C. The number also remained constant when plants were grown in altered nutrient conditions (no sucrose) or in continuous light (Fig. 1G). All of these conditions affect the growth rate of the primary root as evidenced by root length that is considerably reduced by growth at lower temperatures, on media without sucrose, and in continuous light (Fig. 1G). In addition, we examined bending under altered nutrient conditions (no sucrose), and we found that the number of bends after 72 hours of growth was similar to those in the standard conditions (altered: 14.5 ± 2.1, $n = 25$, and standard: 13.6 ± 1.6, $n = 25$). Taken together, our results indicate that both prebranch site formation and root bending are periodic responses that may be regulated by an endogenous clock mechanism.

Auxin is not sufficient to specify prebranch sites. Given the known role of auxin in several stages of LR formation (*9*, *15*, *16*) and the general use of DR5 as an auxin-signaling reporter (*17*), we investigated whether prebranch site formation was related to changes in levels of this hormone. We generated different auxin-signaling reporters by fusing the promoters of INDOLE-3-ACETIC ACID INDUCIBLE 7 (IAA7), IAA14, and IAA19 to the luciferase coding region and tested them for response to exogenous application of auxin in the OZ. pIAA19 was expressed in the OZ and responded to exogenous auxin in a fashion similar to that of DR5:Luciferase (Fig. 2, A and B, and movies S3 and S4), whereas pIAA7 and pIAA14 responded to auxin at later times. When we evaluated the expression of pIAA19 in the OZ without any hormone treatment, we did not detect an oscillatory behavior in its expression over time

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(Fig. 2C and movie S5). Although additional transcriptional regulation of pIAA19 cannot be excluded, our data suggest that fluctuation in auxin is unlikely to be sufficient to drive the periodic pulses of DR5 expression in the OZ.

Induction of auxin biosynthesis in pericycle cells has been linked to acquisition of LR founder-cell identity (*18*). Thus, we tested whether auxin could generate prebranch sites independently of the oscillation reported by DR5. We performed localized auxin treatments in the OZ, both when natural peaks of DR5 expression were detected and when they were not detected. Exogenous auxin treatment or auxin plus 1-*N*-naphthylphthalamic acid (NPA), which should prevent auxin movement, did not lead to production of a prebranch site when the treatment was not concurrent with a DR5 oscillation (Fig. 2, D and E). When the DR5 oscillation was concurrent with application of auxin or auxin plus NPA, the prebranch site appeared to be shifted from the predicted position of a natural prebranch site in ~60% of the cases (Fig. 2E). However, auxin did not seem to specify a new prebranch site, because two prebranch sites were never observed in close proximity after the auxin treatment (fig. S2). As DR5 expression also marks LR founder cells (*18*), this indicates that functional founder-cell specification normally requires the oscillation reported by DR5. However, we cannot rule out the possibility that at very high, sustained doses of auxin there may be de novo production of LRs through a mechanism that does not depend on prebranch site formation.

Additionally, it has been proposed that root bending could promote auxin accumulation preferentially at the outside of the curve, which, in turn, could induce LR formation (*19*, *20*). This was particularly intriguing because we had observed that primary root bending occurred with a frequency similar to that of prebranch site production (Fig. 1, E and F), and prebranch sites tend to be located in the middle of the bends. Thus, we examined whether ectopic prebranch sites were induced by manual bending (generating J-hooks) near the root tip (*19*). When J-hooks were formed ~5 mm from the root tip, the J-hook occurred at a position where prebranch sites were already specified (fig. S3). We found that the first prebranch site was located at an average of 3 mm from the root tip, and we did not detect ectopic formation of prebranch sites at J-hooks (fig. S3). Lateral roots always emerged from preexisting prebranch sites. In addition, we examined gravity-induced bends. We altered the root's position relative to the gravity vector by rotation of either 90° or 180° in the vertical plane or by turning the plants 90° from the vertical to horizontal plane (fig. S4). We observed that gravity-induced bends occurred in an asynchronous manner. Roots rotated 180° showed gravity-induced bending after an average of 3 hours; however, many roots took longer to bend, as seen in the skewed distribution in Fig. 2F. Interestingly, the time between the last periodic bend prior to the 180° rotation and the subsequent gravity-induced bend followed a distribution similar to that detected for roots under normal conditions (Fig. 2F and Fig. 1F). This suggests that the root's natural periodic bends are completed prior to gravity-induced bends. It has been reported that gravistimulation at 6-hour intervals is optimal for increasing LR density (*21*). As LR development requires previous formation

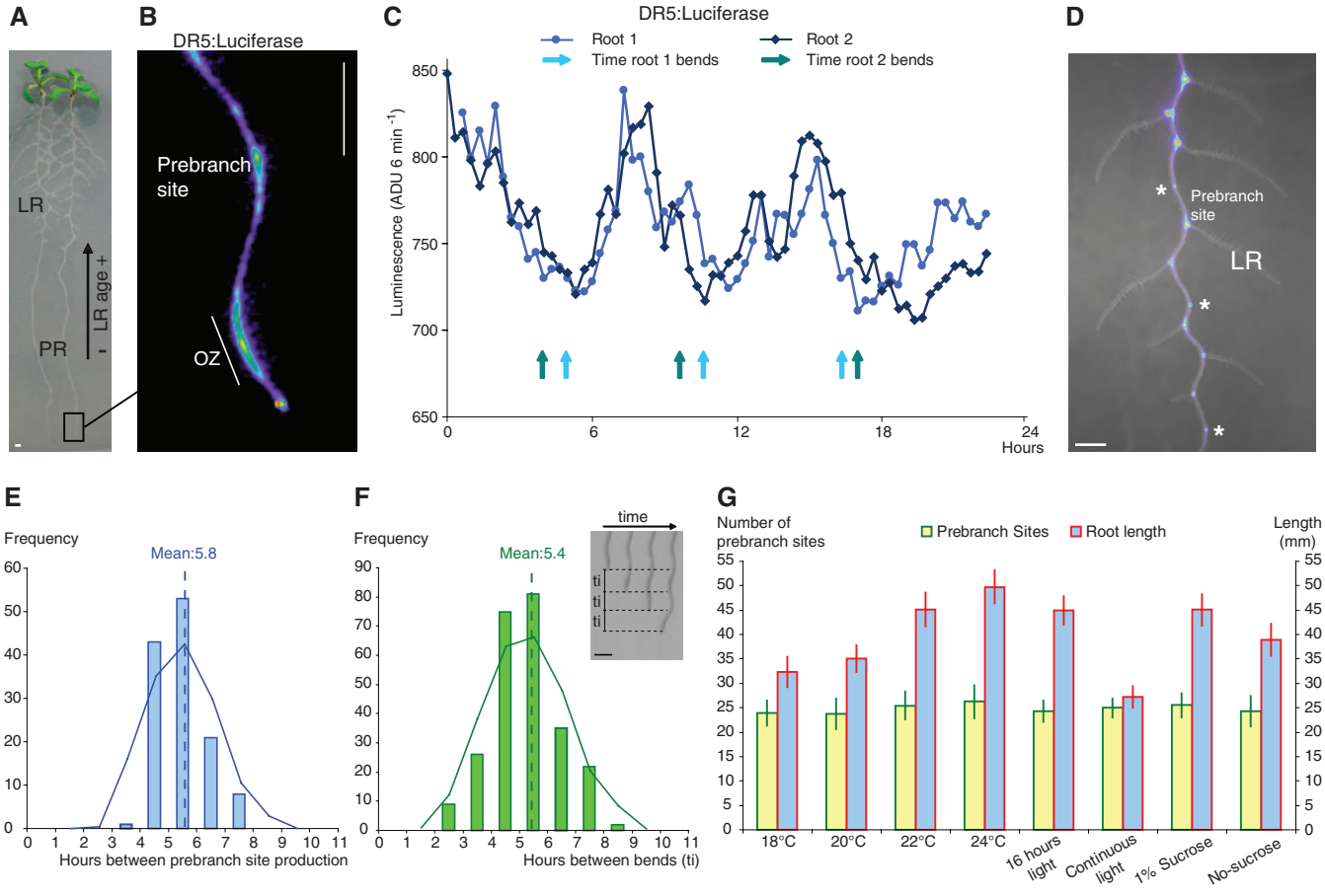

Fig. 1. Periodic branching and bending are marked by repeated pulses of DR5 reporter expression. (**A**) LRs develop from the primary root (PR), and younger LRs are located closer to the PR tip. (**B**) DR5 fused to the luciferase reporter gene is expressed in the oscillation zone (OZ) and prebranch site(s). (**C**) Quantification of DR5 expression in the OZ over time. Arrows mark the time when the primary root bends. (**D**) Overlay of luciferase and bright-field images of a DR5-expressing root. Bright-field image was taken 5 days after the luciferase picture. Asterisks indicate LR primordia that did not emerge. (**E** and **F**) Graph of the distribution of prebranch site production and bending over time (n = 15 and 30, respectively). (Inset) Root bends with time interval (t_i) between bends. (**G**) Prebranch site production and root length under different growth conditions (n = 40). Scale bars, 1 mm.

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of a prebranch site, it is possible that the observed increase in LR density is due to the gravistimulus-promoted development of each prebranch site into a LR primordium. In addition, after rotation of the roots, we detected peaks of DR5 expression approximately every 3 hours; this is more frequent than expected for the periodic DR5 oscillation or the response to gravity alone (Fig. 2G). It has been previously reported that auxin may accumulate following gravity-induced bending (*19*). To examine this further, we observed pIAA19 expression after gravistimulation. We found that pIAA19 peaks of expression were less frequent than peaks of DR5 expression after gravistimulation (Fig. 2H). Because pIAA19 does not oscillate, but responds to auxin, these pIAA19 peaks may report increases in auxin signaling or content due to gravity response. Under gravity response conditions, pulses of DR5 expression generated static points of DR5 expression; however, not all of these points persisted and only a few formed a prebranch site that eventually developed a LR (fig. S4). In addition, we tested whether prebranch site formation was affected by conditions that reduced root bending by growing roots through the growth medium. We detected approximately the same number of prebranch sites for roots that grew through the agar as for roots grown along its surface (standard conditions) (Fig. 2I). This indicates that prebranch site specification occurs in the absence of visible root bends.

Taken together, our results indicate that competence to form a LR through establishment of prebranch sites is determined by internal cues reported by peaks in DR5 expression. Auxin may contribute to this endogenous mechanism, because application of auxin appears to shift the location of a prebranch site. In addition, the root gravitropic response, which likely involves altered endogenous auxin concentrations, appears to be able to change the period of the endogenous mechanism.

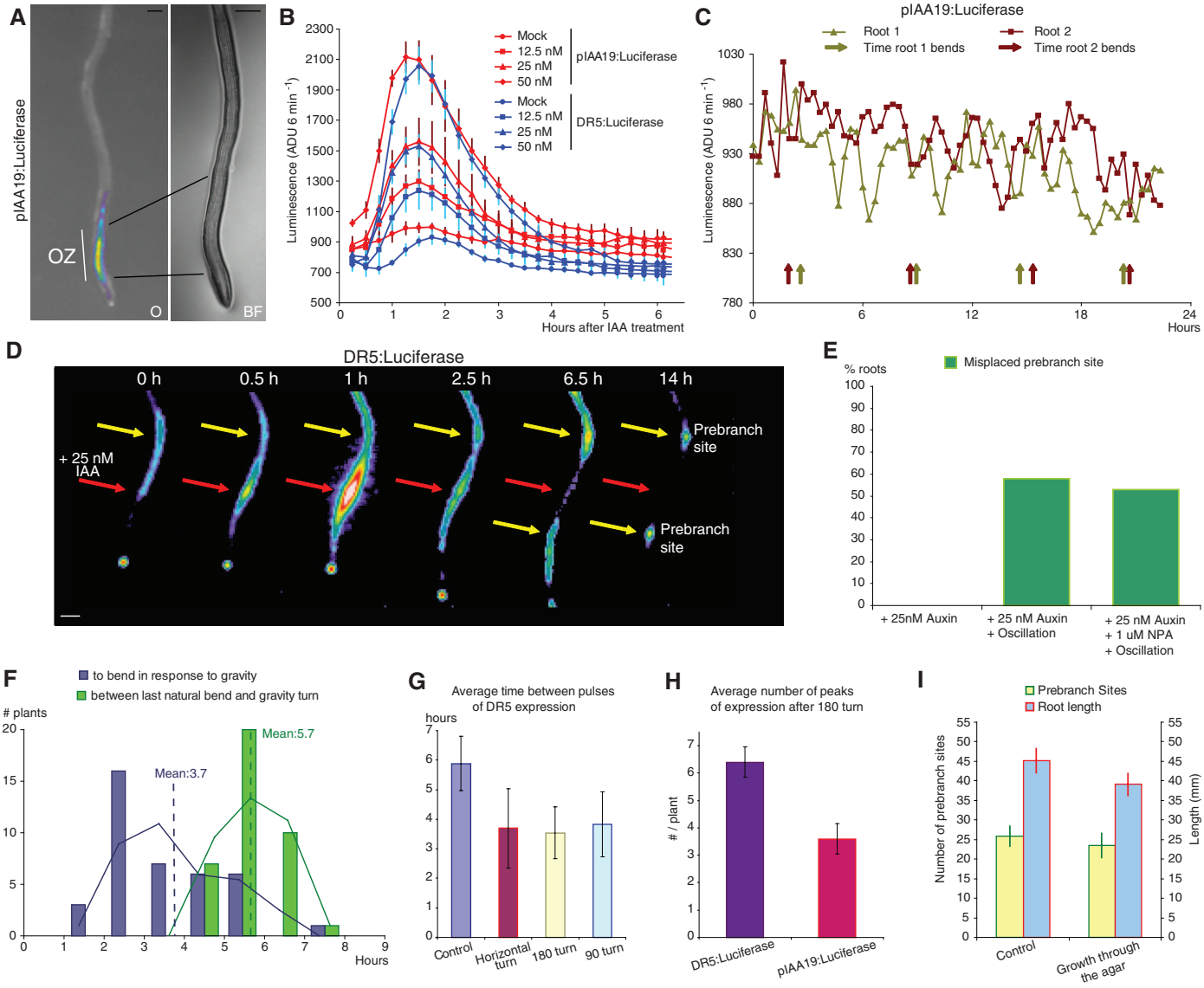

Fig. 2. Manipulation of auxin levels or signaling is not sufficient to induce prebranch site formation or ectopic branching. (**A**) Overlay (O) of bright-field and luciferase images, and detailed bright-field image (BF), showing expression of pIAA19 fused to the luciferase reporter. (**B**) Quantification of pIAA19 and DR5 expression in the OZ after localized auxin treatments (n = 10). (**C**) Quantification of pIAA19 expression in the OZ over time. (**D**) Time series of a DR5:Luciferase-expressing root after OZ-localized auxin treatment. Yellow arrows indicate natural DR5 oscillations. Red arrow shows the location of the auxin treatment. (**E**) Percentage of plants showing misplaced prebranch sites in response to OZ-localized auxin and NPA treatments. (**F**) Distribution of the time to bend in response to gravity after a 180° turn (n = 39). (**G**) Time between consecutive pulses of DR5 expression over a 20-hour period under normal conditions and after changing the relative position of roots to gravity by turning. (**H**) Number of peaks of DR5 or pIAA19 expression detected over a 20-hour period after a 180° turn (n = 10). (**I**) Prebranch site production and root length for roots grown on the surface (control) or through the growth medium (n = 15 for each). Scale bars, 250 μm. Error bars represent SD.

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Genes oscillate in opposite phases before LR initiation. From our previous results, we hypothesized that the periodic behavior of the DR5 reporter in the OZ might represent a more general oscillatory transcriptional mechanism. To determine what genes, if any, were expressed in a periodic pattern similar to that of DR5, we dissected the OZ of 40 individual roots and divided it into an upper (OZ2) and lower (OZ1) half (fig. S5). Because we were unable to synchronize the roots, we analyzed DR5:GUS expression by real-time reverse transcription polymerase chain reaction (RT-PCR) in the two halves of the OZ to infer an approximate chronological order of the different roots along one cycle of the DR5 oscillation (supporting online text). On the basis of the inferred order, we selected 20 OZ1 and 19 OZ2 representative samples and performed microarray experiments on each one (fig. S6). The microarray data from these samples were concatenated to generate an inferred time series. To identify gene expression profiles that exhibited periodic behavior, we used two different pattern-detection methods. One was a modification of the Lomb-Scargle periodogram (*3*), which is related to Fourier transform analysis, and the other was the address-reduction method, which is data-driven and, unlike Lomb-Scargle, does not assume periodicity of the patterns of interest (*22*). Although both methods have been shown to identify known periodic genes within diverse microarray time series (*23*), we considered significant only those genes identified by both approaches and that met other filtering criteria based on fold-change and expression levels (Fig. 3A and table S1). In addition, randomization of the samples showed that substantial numbers of periodic gene expression patterns were only associated with the order given by the analysis of the DR5:GUS expression (fig. S8). Two distinct sets of genes were identified as oscillating in the OZ. One set comprised 2084 genes oscillating in phase with DR5, and the second set was made up of 1409 genes, which oscillated in antiphase to DR5 (Fig. 3B). The predicted oscillating expression pattern of several of these genes in the OZ was validated by constructing fusions of their promoters to the luciferase gene (movies S6 to S10). Quantification of the luciferase activity in the OZ showed that expression of pZAT11 and pARF7 rhythmically pulsed (Fig. 3, C to F) with the same period as DR5 (Fig. 1C).

Analysis of the underlying molecular mechanisms of auxin-mediated LR initiation has been examined by microarray analyses under different experimental conditions (*24*, *25*). To address whether the molecular oscillation in the OZ contained components similar to those previously described for LR initiation, we compared all these data sets (fig. S9). We found little overlap (<15%) between the oscillating genes and the various LR initiation data sets (fig. S9), which suggested that prebranch site production and LR initiation use distinct molecular mechanisms, as would be ex-

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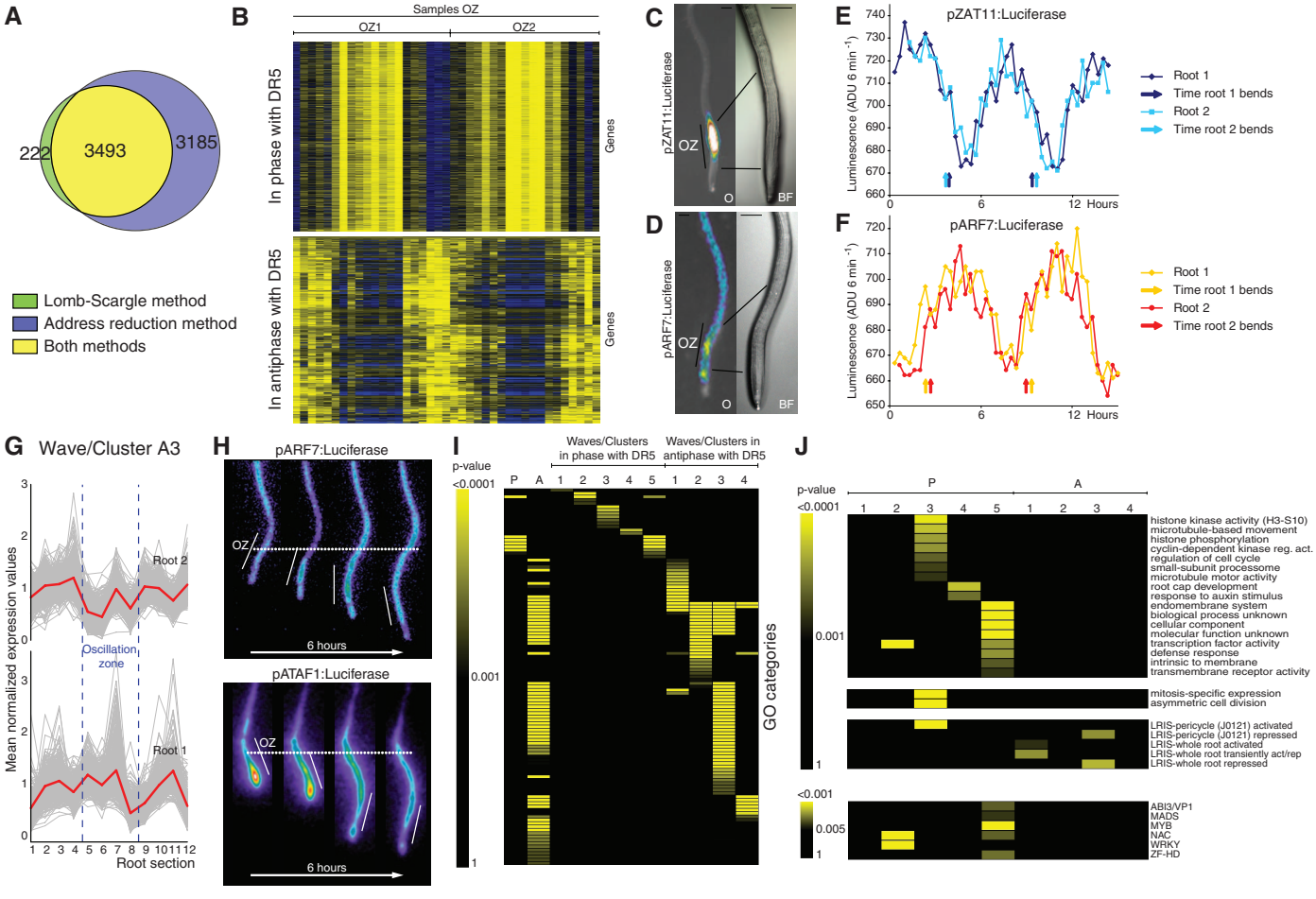

Fig. 3. Identification of genes with periodic expression behavior in the oscillation zone. (**A**) Venn diagram showing the number of genes exhibiting periodic behavior as identified by two different methods. (**B**) Heat maps of the two sets of genes found to oscillate in the OZ. Yellow indicates higher and blue indicates lower relative expression. (**C** and **D**) Overlay (O) of bright-field and luciferase images showing expression of the promoter of (C) ZAT11 in phase with DR5, and (D) ARF7, in antiphase, fused to the luciferase gene. Bright-field images (BF) detailing the OZ are shown to the right (C and D). Scale bars, 250 μm. (**E**) Quantification of pZAT11:Luciferase and (**F**) pARF7:Luciferase expression in the OZ over time. (**G**) Expression profiles for oscillating genes in cluster A3 as expressed in the RootMap. Red line represents average gene expression. (**H**) Time series of pARF7:Luciferase (top) and pATAF1:Luciferase (bottom) expression (cluster A3). Dotted lines mark a fixed spatial position. (**I**) Gene Ontology (GO) term enrichment in the phase (P) and antiphase (A) gene clusters and (**J**) their enrichment in data sets profiling LR initiation and in transcription factor families.

pected for distinct developmental processes. Among the common genes, we found LOB-DOMAIN 16 (LBD16) and LBD33, which have roles in LR initiation (*26*). However, we did not find IAA14-SOLITARY ROOT (SLR), which is required for LR initiation (*27*) but not for establishment of LR primordia (*10*, *27*). One of the genes found only in the OZ data set is AUXIN RESPONSIVE FACTOR 7 (ARF7), which is upstream of LBD16 (*26*); and unexpectedly, OZ-localized auxin treatment did not result in increased expression of pARF7:Luciferase. Thus, it is plausible that the pathways leading to auxin-mediated LR initiation and prebranch site formation are largely independent, although specific molecular connections might ensure coordination of both processes.

Oscillating genes change expression along the primary root. Because we performed the microarray experiments with tissue only from the OZ, we were also interested in examining the behavior of the oscillating genes over developmental time. Recently, a spatiotemporal transcriptional map of the *Arabidopsis* root (the RootMap) identified dominant gene expression patterns that fluctuate over developmental time and from root to root (*28*). We examined the expression of the oscillating genes in the RootMap longitudinal data set (*28*), which separately profiles 12 sections from two independent roots. We performed *K*-means clustering of the phase and antiphase gene expression patterns for one of the roots. The oscillating genes were grouped into five phase gene clusters and four antiphase gene clusters. Gene expression patterns for every cluster coordinately changed when examined in the second root (Fig. 3G, fig. S10, and table S1). Expression analyses of the oscillating genes using promoter fusions to the luciferase gene showed that expression of pARF7, pATAF1, pLBD16, pZAT11, and pWRK65 expression changed both across developmental zones and over time in the *Arabidopsis* root (Fig. 3H, fig. S11, and movies S6 to S10). Gene expression also seems to move spatially, propagating along the root's longitudinal axis (Fig. 3H; note that pARF7 and pATAF1 expression moves across the dotted lines). This movement might involve some cell-to-cell communication or signaling process. It is possible that different waves of gene expression might link prebranch site formation with other developmental processes. For instance, ATAF1, in wave A4, has been described as negatively regulating the expression of stress-responsive genes (*29*), and VND6 in wave P2 has been shown to be involved in metaxylem specification (*30*).

To investigate the possible biological functions of these waves of gene expression, we analyzed Gene Ontology (GO) term enrichment (*28*). We found that genes oscillating in opposing phases show significant enrichment in different GO categories and that different waves tend to be enriched in GO categories associated with specific biological processes (Fig. 3I and table S2). Particularly intriguing was the P3 wave (Fig. 3J), which was enriched in GO categories associated with cell cycle progression, mitosis-specific expressed genes, and genes putatively involved in asymmetric division (*24*). Formation of LR primordia requires that LR founder cells undergo a series of asymmetric divisions (*7*), and although progression through the cell cycle has been shown to be involved in LR initiation (*31*), it is not sufficient to specify new LR primordia (*10*, *25*, *27*). Thus, genes within the P3 wave may be required before LR initiation. In accordance with this, we found that most of the genes in common between the OZ data set and the LR initiation data set are in waves P3 and A1 (Fig. 3J and table S3).

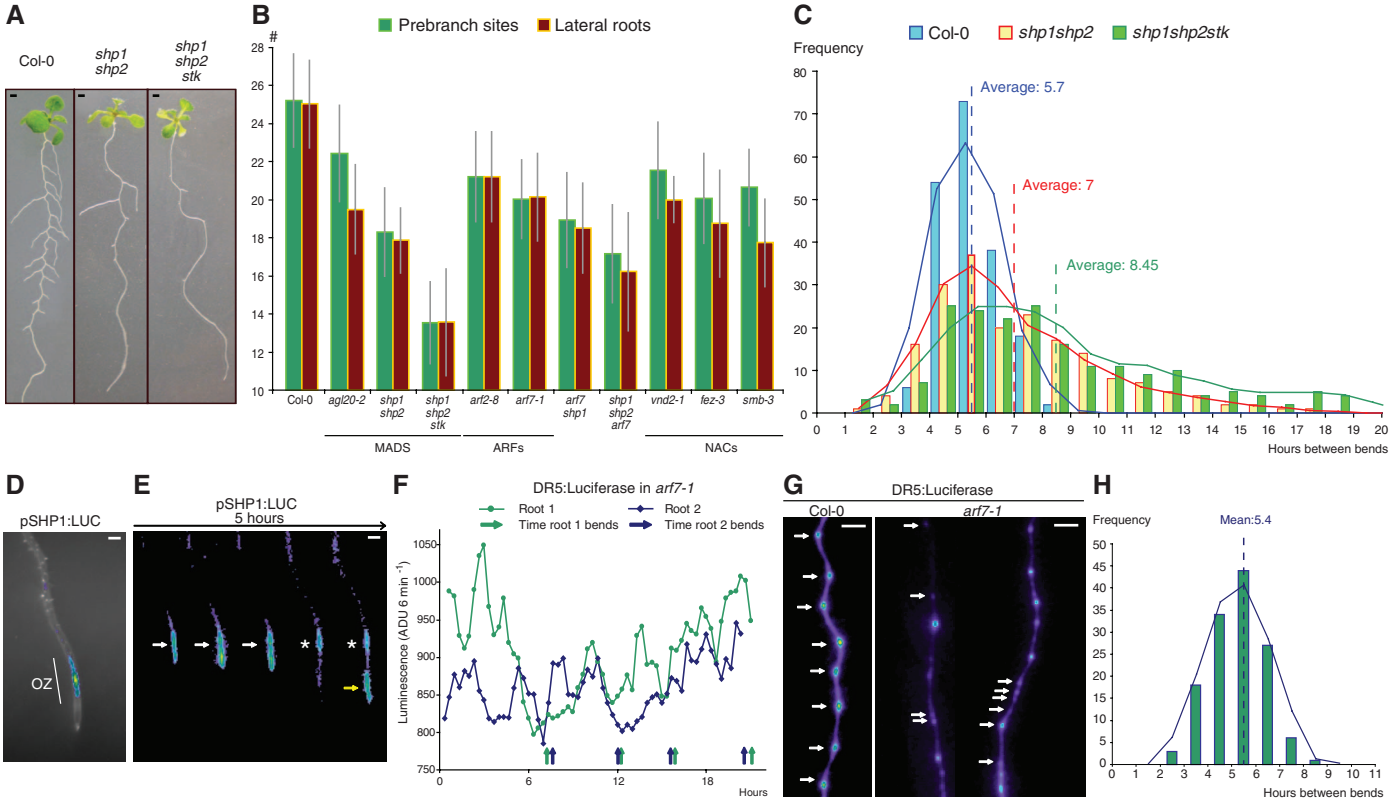

Fig. 4. Oscillating genes encoding transcription factors are necessary for regular prebranch site formation and root bending. (**A**) Bright-field images of seedlings showing root bending and emerged LRs of wild type (Col-0) and mutants. (**B**) Quantification of the number of prebranch sites and LRs for a variety of genotypes ($n = 25$). Error bars, SD. (**C**) Distribution of bending over time in Col-0 compared with mutants ($n = 25$). Note the increased distribution of time between bends in the mutants. (**D** and **E**) Expression of pSHP1:Luciferase in the OZ. (D) Bright-field and Luciferase images overlaid. (E) Time series showing SHP1 expression pulses over time. White and yellow arrows mark first and second expression pulses, respectively; asterisk marks position of a future LR primordium. (**F**) Quantification of DR5:Luciferase expression in the OZ in *arf7-1* mutants. Arrows indicate the times when primary root bending occurred. (**G**) Luciferase images of Col-0 (wt) and *arf7-1* expressing the DR5:Luciferase reporter. White arrows mark prebranch sites. (**H**) Quantification of the frequency of bending in *fez-3* mutants ($n = 15$). Bending of *fez-3* and wild type is similar [compare with (C)]. Scale bars: (A and G), 1 mm; (D and E), 250 μm.

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Oscillating transcription factors regulate root periodic responses. The identification of two main sets of genes oscillating in opposite phases in the OZ suggested that an oscillatory network might be involved in establishing the pace of periodic branching and bending in the *Arabidopsis* root. To further investigate this hypothesis we focused on determining the role of transcription factors (TFs) in regulating root periodic responses. Wave P5 was enriched in genes with an unknown biological function and in transcription factor activity, which suggested that oscillating TFs in wave P5 could be involved in periodic prebranch site formation and bending in the *Arabidopsis* root. Particularly intriguing was the overrepresentation of TFs from the MADS-box protein family (Fig. 3I and table S3) as they have not been described to have a role in root development. Among these TFs were SHATTERPROOF1 (SHP1), SHATTERPROOF2 (SHP2), and SEEDSTICK (STK), which are involved in carpel and ovule development and seed dispersal (*32*), and AGAMOUS-LIKE20 (AGL20), which regulates the transition to the reproductive stage (*33*). Notably, *shp1shp2* and *shp1shp2stk* mutant plants showed striking root phenotypes when compared with the wild type (Fig. 4A). When we examined LR and prebranch site production in *agl20-2*, *shp1shp2*, and *shp1shp2stk*, we observed a substantial decrease in both the total number of LRs and prebranch sites as reported by DR5 (Fig. 4B). These defects were not related to delayed seed germination in the mutants. Furthermore, analysis of the time between consecutive bends showed that periodic bending was also defective in *shp1shp2* and *shp1shp2stk* (Fig. 4C). Using a transcriptional reporter, we found that expression conferred by the SHP1 promoter fluctuated over time in the OZ (Fig. 4, D and E) and that it appeared transiently in static points of expression resembling prebranch sites (Fig. 4E). Examination of these points microscopically after 1 day revealed early stages of LR primordia. Our results indicate that MADS-box TFs are involved in periodic processes in the *Arabidopsis* root.

Additionally, we screened T-DNA insertion lines for 55 oscillating transcription factors identified in our data set. Several TFs belonging to the ARF (ARF7 and ARF2) and NAC [VND2, FEZ, and SOMBRERO (SMB)] families showed defects in prebranch site initiation and reduced numbers of LRs (Fig. 4B). In addition, the double and triple mutants *arf7shp1* and *arf7shp1shp2* showed some reduction and increased variability in the number of prebranch sites compared with *arf7* and *shp1shp2*, respectively. These findings indicate that there is some genetic interaction between ARF7, SHP1, and SHP2, which suggests that these TFs may function in the same pathway to periodically produce prebranch sites. In *arf7* plants, we observed that DR5 expression in the OZ was more persistent compared with wild-type plants and lacked periodicity (Fig. 4F), resulting in irregular locations of prebranch sites along the primary root (Fig. 4G). This suggests a role for ARF7 in regulation of periodic oscillating gene expression leading to prebranch site formation.

We observed that *fez-3* mutants were impaired in prebranch site formation (Fig. 4B), but quantification of the time between bends showed a distribution similar to that in wild-type plants (Fig. 4H). This indicates that prebranch site formation and bending can be genetically separated and that these two periodic processes may be regulated by different sets of genes. Taken together, our results strongly suggest that an oscillatory network located in the OZ is the endogenous developmental mechanism triggering periodic branching and bending in the *Arabidopsis* root.

Discussion. How plants position newly formed organs during postembryonic development is a major unanswered question. In the root, this requires that subsets of cells be specified to generate LR primordia. We present evidence that in the *Arabidopsis* primary root, a process involving oscillating gene expression, which has characteristics of a biological clock, is the first step in positioning new LRs. This temporal prepatterning mechanism results in establishment of prebranch sites, which determines the position from which LRs will develop. Auxin may contribute to this process, but it does not appear to be sufficient to initiate a prebranch site. In addition, subsequent effects of auxin on modulating LR emergence likely participate in the final LR spatial distribution pattern. Remarkably, the root's response to gravity seems to affect the period of the endogenous mechanism producing prebranch sites. The integration of external cues with an endogenous developmental mechanism may represent an advantage for plants growing in soil where roots are forced to bend in response to various obstacles. In this case, branching in precise locations would maximize the root system's ability to explore heterogeneous territory for resources to support overall plant growth.

Current models for shoot phyllotactic patterning indicate that auxin accumulation controls the spatial patterning of aerial organs (*34*). In contrast, oscillating gene expression in the OZ of the *Arabidopsis* root seems to be responsible for establishing the spatial-temporal distribution of LR primordia. Remarkably, this shares similarities with the segmentation clock in vertebrates, where a large network of genes with oscillating expression in the presomitic mesoderm has been described (*5*). Somite length and number is temperature-compensated (*35*), whereas there is temperature compensation of the period of prebranch site production. In animals where development results in a fixed body plan, maintenance of somite size and number would be critical; however, in plants where the final body axis is flexible, a fixed production rate might optimize the root system's exploration of the soil. Thus, it appears that independently evolved multicellular organisms have converged upon analogous mechanisms to position modular units along specific growing axes.

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Supporting Online Material

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Movies S1 to S10

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A Transient and Low-Populated Protein-Folding Intermediate at Atomic Resolution

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Proteins can sample conformational states that are critical for function but are seldom detected directly because of their low occupancies and short lifetimes. In this work, we used chemical shifts and bond-vector orientation constraints obtained from nuclear magnetic resonance relaxation dispersion spectroscopy, in concert with a chemical shift–based method for structure elucidation, to determine an atomic-resolution structure of an "invisible" folding intermediate of a small protein module: the FF domain. The structure reveals non-native elements preventing formation of the native conformation in the carboxyl-terminal part of the protein. This is consistent with the kinetics of folding in which a well-structured intermediate forms rapidly and then rearranges slowly to the native state. The approach introduces a general strategy for structure determination of low-populated and transiently formed protein states.

There is increasing evidence that metastable intermediates are ubiquitous along protein-folding pathways (*1*–*7*). Because they are transiently formed and weakly populated, the detection and characterization of these excited states remains a challenge. Recent developments in relaxation dispersion nuclear magnetic resonance (NMR) spectroscopy provide an opportunity for detailed study of such rare states (*5*, *8*, *9*). Although they cannot be detected in NMR spectra, the presence of these "invisible" conformers nevertheless leads to broadening of peaks derived from nuclei within the "visible" ground-state structure. Such excess line broadening can be quantified, providing that conformers in the ground state exchange with those in the excited state on the millisecond timescale with fractional excited-state populations of at least 0.5% (*10*). In this case, by recording the decay rate of transverse magnetization $R_{2,\mathrm{eff}}$ (Fig. 1A) as a function of the strength of an applied radio-frequency field (ν_{CPMG}), it is possible to extract the kinetics and thermodynamics of the exchange process, as well as the chemical shifts of the ^{1}H, ^{13}C, or ^{15}N probed nuclei (*8*, *11*). In a related class of experiments recorded under conditions of weak molecular alignment, residual dipolar couplings (RDCs) that report on the relative orientation of bond vectors in the excited state can be measured (*12*, *13*).

Previously, our laboratory has inferred structural properties of low-populated folding intermediates by comparing limited numbers of NMR chemical shifts of the intermediate with the corresponding shifts that are predicted for an unfolded, random coil ensemble (*5*, *14*, *15*). However, obtaining an extensive set of chemical shifts and bond-vector orientations (*8*, *9*) opens the possibility of calculating detailed three-dimensional (3D) atomic-resolution models of invisible excited states (*16*). Central to the structure calculations is the emergence of robust computational protocols that do not rely on experimental distance restraints, but instead employ backbone chemical shifts in concert with structural databases (*17*–*19*). Accurate structures for ground states of small proteins on the order of 120 residues or less are obtained in this manner. We have used backbone ^{15}N, $^{1}H^{N}$, $^{13}C^{\alpha}$, $^{1}H^{\alpha}$, and $^{13}C^{O}$ chemical shifts, as well as amide bond-vector orientations, to generate a structure of an invisible folding intermediate of the wild-type (WT) FF domain from HYPA/FBP11 (*20*) with an equilibrium population of 2 to 3% and a millisecond lifetime.

Relaxation dispersion measurements. The FF domain from HYPA/FBP11 is a small 71-residue, four-helix bundle with H1(α)-H2(α)-H3(3_{10})-H4(α) topology (*20*) that folds by a three-state mechanism involving an on-pathway intermediate (I): U ↔ I ↔ N (*14*, *21*–*23*). Folding proceeds in two phases, including the fast formation of I from the unfolded state U (microsecond time scale) and a slower, rate-limiting transition from I to the na-

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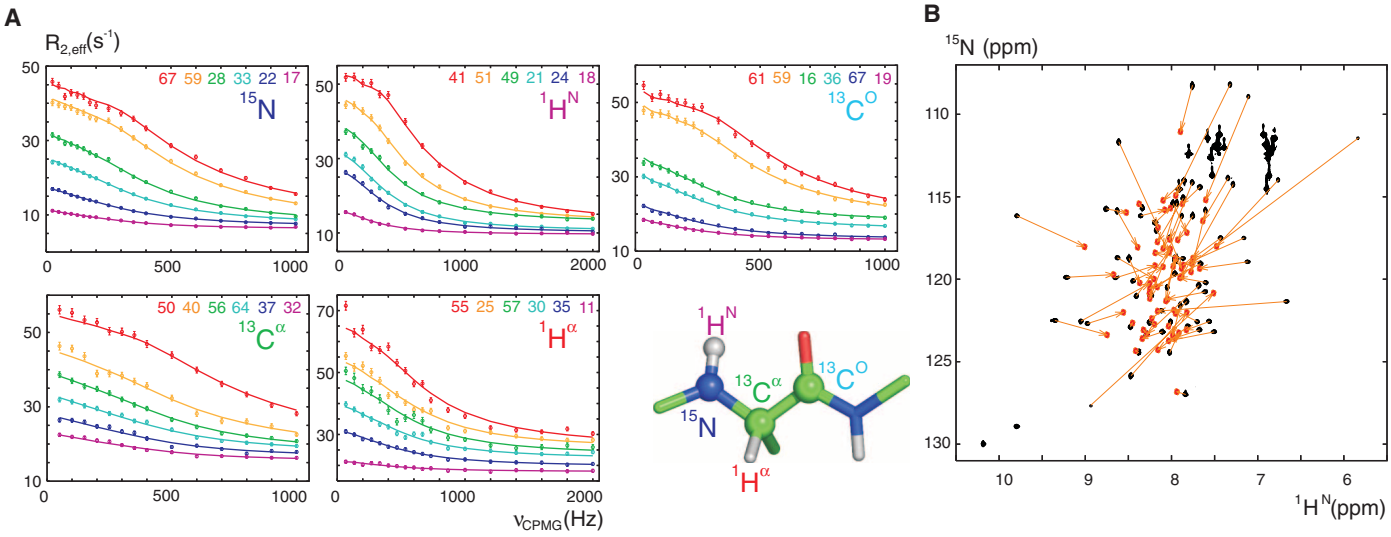

Fig. 1. Probing the invisible intermediate state by relaxation dispersion NMR. (**A**) Experimental relaxation dispersion profiles for select backbone ^{15}N (*12*, *26*), $^{1}H^{N}$ (*27*), $^{13}C^{\alpha}$ (*11*), $^{1}H^{\alpha}$ (*29*), and $^{13}C^{O}$ (*11*, *30*) nuclei of the WT FF domain ($FF_{1\text{-}71}$) measured at a static magnetic field of 18.8 T (open circles), along with best fits to a two-site exchange model, I ↔ N, performed as described elsewhere (solid lines) (*5*). Residue numbers are shown in the top right corner of each box. Error bars indicate uncertainties in $R_{2,\mathrm{eff}}$ rates. The experiments made use of protein samples with specifically tailored isotope labeling schemes [U-^{15}N,^{13}C,^{2}H-labeling for ^{15}N, $^{1}H^{N}$, $^{13}C^{O}$ dispersion experiments, 30°C; selective-$^{13}C^{\alpha}$ labeling, full protonation (*49*) for $^{13}C^{\alpha}$ experiments, 30°C; U-^{15}N,^{13}C, ≈50%-^{2}H labeling (*29*) for $^{1}H^{\alpha}$ experiments, 35°C], and the data were analyzed separately for each type of nucleus as described in (*32*). The extracted values of $\Delta\varpi_{\mathrm{IN}}$, with signs of chemical-shift differences determined as described previously (*33*, *50*), are used for calculating the chemical shifts of the invisible intermediate, $\varpi_{\mathrm{I}} = \varpi_{\mathrm{N}} + \Delta\varpi_{\mathrm{IN}}$, allowing reconstruction of its NMR spectra. The reconstructed ^{15}N,$^{1}H^{N}$ correlation map of the I state (orange) and the experimental spectrum of the N state (black) are shown in (**B**). ppm, chemical shifts in parts per million.

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tively folded state N (millisecond time scale) (*21*). The transition state between I and N has been characterized previously by Φ-value analysis (*24*) with 50 mutations, establishing that this state contains a structured core centered at the end of H1 and the beginning of H2 (*22*).

We performed a series of NMR relaxation dispersion experiments focusing on ^{15}N, $^{1}H^{N}$, $^{13}C^{\alpha}$, $^{1}H^{\alpha}$, and $^{13}C^{O}$ nuclei of the protein backbone (Fig. 1A) (*11*, *12*, *25*–*30*). In a previous study of the folding of $Ala^{17} \rightarrow Gly^{17}$ (A17G) and Q19G (*31*) mutant FF domains, ^{15}N relaxation dispersion data could only be properly fit with the use of a model of three-site exchange with an on-pathway intermediate (*14*). However, for the WT domain, the U ↔ I transition could not be detected due to the extremely fast rate of interconversion between these states (*21*) and the low population of U relative to I [$p_U/p_I < 0.2$, based on hydrogen-deuterium exchange data (*14*), where p_U and p_I are fractional populations of states U and I, respectively]. Consistent with this finding, the dispersion data in this study were well fit, assuming a model of two-state exchange, $I \underset{k_{N\rightarrow I}}{\overset{k_{I\rightarrow N}}{\rightleftharpoons}} N$, where $k_{I\rightarrow N}$ and $k_{N\rightarrow I}$ are rate constants [see the supporting online material (SOM)] (*32*). This allowed extraction of the population p_I, the exchange rate constant $k_{ex} = k_{N\rightarrow I} + k_{I\rightarrow N}$, and absolute values of chemical-shift differences between states $|\Delta\varpi_{IN}|$. From $|\Delta\varpi_{IN}|$, the chemical shifts $\varpi_I = \varpi_N + \Delta\varpi_{IN}$ were subsequently obtained (*33*) for more than 90% of the possible backbone resonances in the protein. We performed ^{15}N experiments at 30°C using a uniformly ^{15}N,^{13}C,^{2}H-labeled sample in H_2O buffer, which gave $p_I = 2.84 \pm 0.02\%$ and $k_{ex} = 1817 \pm 14\ s^{-1}$, with some variation in p_I and k_{ex} for samples dissolved in $^{2}H_2O$ ($^{1}H^{\alpha}$ dispersion experiments) or fully protonated ($^{13}C^{\alpha}$ experiments). Figure 1B compares ^{15}N,$^{1}H^{N}$ spectra of the visible N state (black) with the reconstructed data set of the invisible intermediate (orange) on the basis of chemical shifts extracted from fits of the dispersion data.

We obtained backbone $^{1}H^{N}$-^{15}N RDCs (92% of residues) by recording dispersion experiments under conditions of fractional protein alignment (*12*, *34*). Together, the backbone chemical shifts and amide RDCs constitute the experimental data that we used to calculate structures of the WT FF folding intermediate.

Secondary structure and flexibility of the intermediate state from chemical shifts. Chemical shifts are very sensitive probes of local protein conformation from which protein secondary structure can be determined (*35*). They also report on protein flexibility that can be empirically estimated by the random coil index (RCI) method (*36*). We have used ϖ_I values to initially assess secondary structure and dynamics of the folding intermediate.

The secondary structures of the N and I states of the FF domain predicted from backbone chemical shifts using the TALOS+ program (*37*) are highlighted in Fig. 2A, superimposed on the tertiary folds of these states that were generated by standard NMR methods [N state (*20*)] or by using the approach detailed below (I state). Not surprisingly, TALOS+ correctly identifies the four helices, H1 to H4, of the native state. The intermediate also comprises four helices, and H1 and H2 have similar boundaries to those observed in the native state. However, the third helix of the intermediate is non-native, spanning residues Arg^{48} (R48) to L55 (*31*) that form the 3_{10}-helix H3, the H3-H4 loop, and the beginning of H4 in the native protein. The fourth (and C-terminal) helix in the intermediate, extending from K59 to K66, is not as well defined as the other helices.

Squared order parameters (S^2), measuring amplitudes of motion for the backbone amide groups, obtained by the RCI approach (*36*) clearly suggest that the intermediate state has a well-structured core of ~45 residues that includes helices H1 to H3, flanked by more flexible N- and C-termini (Fig. 2B). Notably, the predicted order parameters for helices H1 to H3 are similar in the I and N states, with S^2 values between 0.7 to 0.9 for the intermediate, although the loop between H1 and H2 and the C terminus of H3 are more dynamic. Finally, S^2 values of ≈0.6 are obtained for residues in helix H4 of the intermediate, suggesting that this element is less stably formed in the I state, which is consistent with previously reported hydrogen-deuterium exchange data (*14*).

Structure determination of the folding intermediate by CS-Rosetta. Recently, substantial progress has been achieved in the development of computational approaches for de novo protein structure determination in which short protein fragments that are compatible with experimental chemical shifts are selected from a structural database and subsequently assembled into 3D models (*17*–*19*). Structures of proteins smaller than ~120 residues calculated in this manner have an accuracy better than 2 Å. The methodology can be further extended to larger proteins in cases where small numbers of backbone distance restraints can be measured (*38*); unfortunately, this is not possible presently in studies of invisible excited states. In this work, we have made use of one such chemical shift–based method for structure determination, CS-Rosetta (*18*, *39*). We have modified the scoring function during the final structure-selection stage to include residuals between predicted and measured RDC values in addition to the Rosetta energy that has been rescored to include experimental chemical shifts, as described previously (*18*) (see SOM materials and methods). The protocol was first tested using backbone ^{1}H, ^{13}C, and ^{15}N chemical shifts of the native WT FF domain, ϖ_N. An accurate model of the native state was generated with a 1.4 Å backbone root-mean-squared deviation (RMSD) to the experimentally determined NMR structure (*20*) and with correctly packed side chains (fig. S1).

We performed calculations of structures of the I state for residues 11 to 66 that exclude flexible N- and C-termini that may adversely affect the convergence of the CS-Rosetta protocol (*18*). Figure 3A shows the typical funnel-like shape of the CS-Rosetta energy function versus RMSD to the lowest-energy structure that is characteristic of converged structure calculations. The structures produced are well defined with a mean pairwise backbone RMSD among the 10 lowest-energy structures of 1.1 Å calculated for residues with $S^2 > 0.7$ (see SOM materials and methods). Although RDC values have been included in the final scoring function for "rigid" residues, very similar structures are obtained, irrespective of whether such restraints are used. The mean RMSD between backbone-heavy atoms of structures calculated with and without RDC values is 1.25 Å for residues with $S^2 > 0.7$, and the lowest-energy conformers in each set of structures are identical.

Calculated intermediate-state structures are in excellent agreement with the input experimental data. For example, the overall lowest-energy model of the intermediate state is in the top 3, 0.2, and 0.2% of all structures based on Rosetta, chemical-shift, and RDC energies, respectively. Figure 3, B

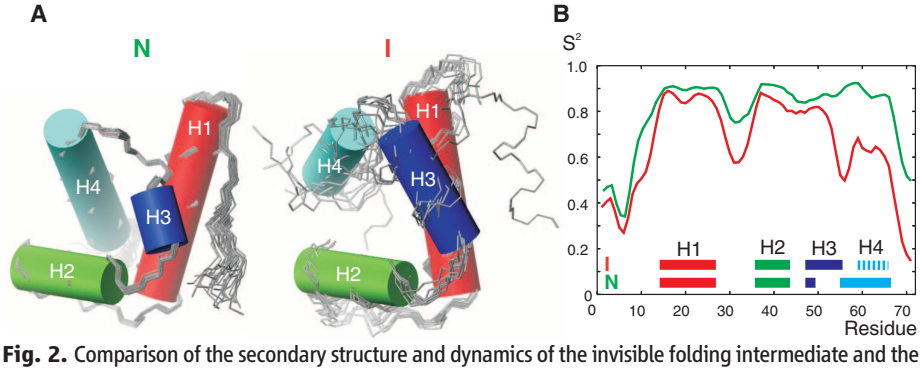

Fig. 2. Comparison of the secondary structure and dynamics of the invisible folding intermediate and the native state of the WT FF domain. (**A**) Helix boundaries are as predicted by TALOS+ (*37*) based on a nearly complete set of backbone chemical shifts: 14 to 27, 36 to 43, 48 to 49, and 54 to 67 in the native state and 14 to 27, 36 to 43, 48 to 55, and 59 to 66 in the intermediate. The helices are depicted by rods superimposed onto an ensemble of the NMR-derived structures of the native state (N) [PDB accession code 1UZC (*20*)] or onto an ensemble of 10 representative structures of the intermediate (I), calculated by CS-Rosetta (*18*). (**B**) S^2 values for the backbone amide groups of the folding intermediate (red) and native state (green), as predicted by the RCI approach (*36*).

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and C, show that a high level of agreement is obtained between experimental chemical shifts and RDC constraints and the corresponding values generated by averaging over shifts and RDCs predicted from each of the 10 lowest-energy structures. The excellent correlation between experimental and calculated chemical shifts provides a measure of confidence in the calculated secondary structure and, to some extent, tertiary interactions, whereas the agreement between measured and predicted RDCs for residues in H1 to H3 indicates that the relative orientation of these helices is correctly captured. In contrast, measured and calculated RDC values for H4 agree much less well with each other, consistent with the fact that this helix is dynamic and only partially formed. RDC values in the intermediate state span a range of more than 100 Hz, several times larger than for the native state. This indicates that the intermediate interacts more extensively than the native state with the polyethylene glycol/hexanol medium (*40*) used for protein alignment, perhaps due to the disordered H4 that would have greater accessibility to the alignment medium.

Structure of the intermediate reveals details of the folding pathway. Figure 4 compares the lowest-energy intermediate and native-state structures. As predicted from S^2 parameters, the intermediate has a well-defined core of ~45 residues that includes α helices H1 to H3. The poorly defined helix H4 has a preferential orientation similar to that of the native H4. The orientations and lengths of helices H1, H2, and the intervening loop are also similar in both states. As predicted by TALOS+, α helix H3 is non-native, including residues that make up helix H3, the H3-H4 loop, and the beginning of α helix H4 in the native structure. Thus, it is not possible for a nativelike H4 to form. The longer H3 docks against H1, and the H1-H3 interface in the intermediate state comprising residues A17, A20, L24 of H1, and L52, L55 of H3 forms interactions distinct from those in the native protein. Additional non-native interactions in the intermediate state are observed at the interface of α helices H2 and H3 involving a hydrophobic cluster consisting of A53, Y49, and I44.

Thus, a substantial number of non-native interactions must be broken before formation of the native conformation, which is probably the reason why the I-to-N transition is rate-limiting for FF domain folding. The model for the intermediate state produced here also provides a structural basis for understanding results from a previous Φ-value analysis of the rate-limiting transition state (*22*). That study concluded that secondary and tertiary interactions are fully formed (large Φ values) only in a relatively small region of the protein including the end of α helix H1, the H1-H2 loop, and the beginning of helix H2. This is the part of the FF domain that is structurally conserved between the I and N states. In contrast, low Φ values were observed for both A17G and A20G mutations in the beginning of H1 and for A51G and L52A in the H3-H4 loop of the native state that is part of helix H3 in the intermediate. The structures of I and N, together with the previous Φ-value analysis (*22*), establish that non-native contacts formed by these residues must be broken between the intermediate state and the rate-limiting transition state along the folding pathway.

A mimic of the intermediate by selective destabilization of the native state. The primary difference between the I and N states of the FF domain is the non-native α helix H3 that prevents formation of the native C-terminal helix H4 that, in turn, is essential for stabilizing the native structure (*20*, *22*). For example, the F62A mutation leads to a completely destabilized domain (*22*). Low $^1H/^2H$-exchange protection factors for the backbone amide groups (*14*) and enhanced flexibility predicted by the RCI approach (Fig. 2) (*36*) suggest that the C-terminal region of the FF domain is at least partially disordered in the intermediate and, therefore, probably only marginally affects the stability of the I state. This suggests that a strategy for selective destabilization of the native state and isolation of a mimic of the folding intermediate might be to cut off the C-terminal part of the protein that includes the native α helix H4.

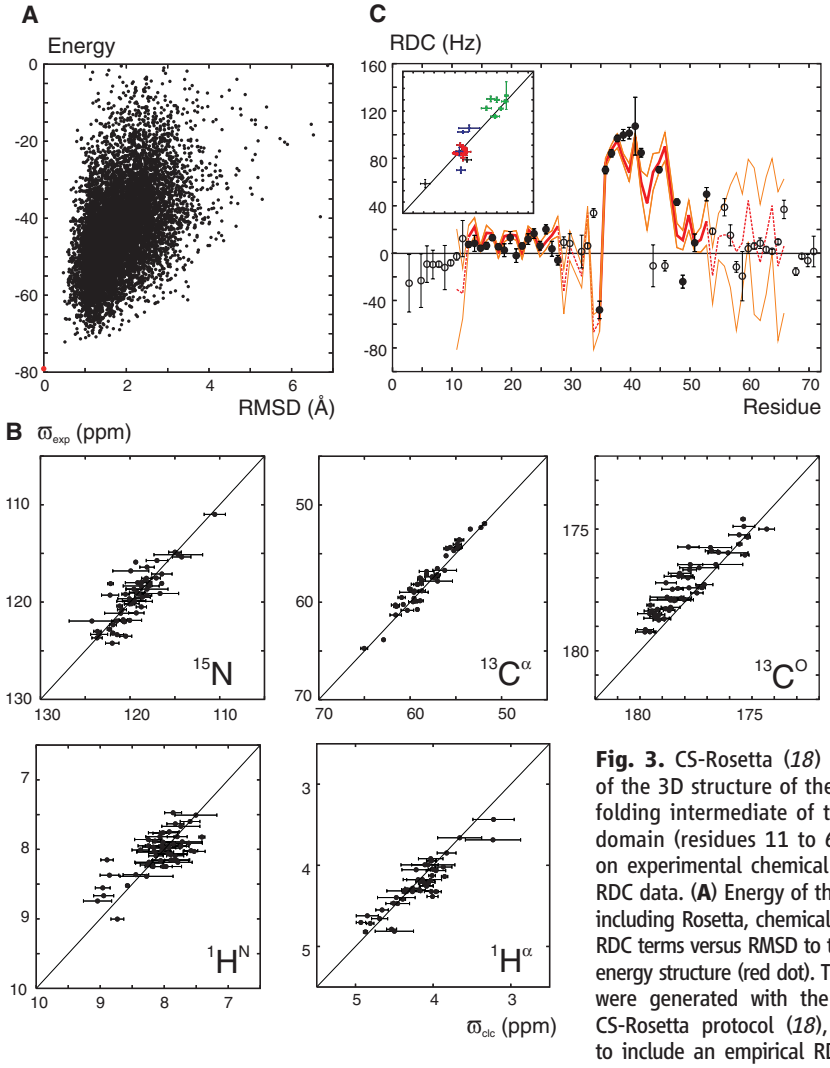

Fig. 3. CS-Rosetta (*18*) modeling of the 3D structure of the invisible folding intermediate of the WT FF domain (residues 11 to 66) based on experimental chemical shift and RDC data. (**A**) Energy of the models, including Rosetta, chemical-shift, and RDC terms versus RMSD to the lowest-energy structure (red dot). The models were generated with the standard CS-Rosetta protocol (*18*), modified to include an empirical RDC energy term at the final stage of re-scoring the calculated structural models. Ten thousand models of the intermediate were generated, of which the 10 with the lowest energies were analyzed. (**B**) Correlation plots of experimental ^{15}N, $^{1}H^{N}$, $^{13}C^{\alpha}$, $^{1}H^{\alpha}$, and $^{13}C^{O}$ chemical shifts of the WT intermediate, ϖ_{exp}, versus chemical shifts predicted by the SPARTA program (*51*), ϖ_{clc}, averaged over an ensemble of the 10 lowest-energy models. The distributions of calculated chemical shifts in the ensemble (1 SD) are indicated by horizontal lines (error bars). (**C**) Plots of experimental (circles) and back-calculated (red lines) $^{1}H^{N}$-^{15}N RDC values averaged over the 10 lowest-energy intermediate structures, as well as the standard deviation in predicted RDC values (orange lines). RDC data for residues with RCI $S^2 > 0.7$ used in scoring of the assembled models are shown by filled circles/solid lines, whereas measured RDC values for residues with $S^2 < 0.7$ or with large uncertainties are indicated by open circles. The dashed red line denotes the average over RDC values calculated for each structure of the ensemble for residues that were not restrained by dipolar couplings in the calculations. (Inset) Experimental RDC values for the core residues (helix H1, red; H2, green; H3, blue) plotted versus back-calculated values averaged over an ensemble of the 10 best structures. Errors in experimental RDC values are indicated by vertical bars, whereas the distributions in the calculated RDC values from the ensemble (1 SD) are indicated by horizontal lines.

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With this in mind, we expressed and purified a variant WT FF domain that includes residues 1 to 60: FF_{1-60} (referred to as I′). This truncated version displays a cooperative thermal-denaturation transition (*41*) with a melting temperature T_m of 39.3 ± 2.8°C and a denaturation enthalpy $\Delta H_{U\text{-}I'}$ (T_m) = 14.2 ± 0.9 kcal/mol (Fig. 5A). The presence of a cooperative transition suggests that FF_{1-60} is well folded and not a large collection of structurally heterogeneous molecules, consistent with expectations for a mimic of the intermediate state. Laser-induced temperature-jump experiments (*23*, *42*) from 22° to 25°C indicate that the truncated FF domain folds with a single kinetic phase $k_{U\rightarrow I'} \sim 10^5\ s^{-1}$ (Fig. 5B), which corresponds to the fast (microsecond–timescale) formation of the folding intermediate in the full-length domain (*21*, *23*).

Although prone to aggregation, the truncated FF domain is amenable to triple-resonance NMR studies that provide backbone ^1H, ^{15}N, and ^{13}C resonance assignments (*43*, *44*). Figure 5C shows the correlation of ^{15}N, $^1H^N$, $^{13}C^\alpha$, $^1H^\alpha$, and $^{13}C^O$ chemical-shift differences between FF_{1-60} and the native full-length domain FF_{1-71} ($\Delta\varpi_{spec}$), with chemical-shift differences between intermediate and native states of FF_{1-71} obtained from relaxation dispersion data ($\Delta\varpi_{disp}$). The chemical shifts of FF_{1-60} and the transiently populated intermediate are quite similar, except for a few residues located proximal to the site of truncation. Therefore, the designed variant must have a structure nearly identical to that of the folding intermediate of the full-length WT FF domain. The quality of the nuclear Overhauser effect spectroscopy (NOESY) spectrum recorded for FF_{1-60} does not permit a detailed structural characterization of this truncated domain. Whereas there are cross-peaks at ^1H methyl frequencies connecting A17 and A20 with L52(δ1 and δ2) and L55(δ1) that form the non-native interface between helices H1 and H3 in the intermediate state, potential overlap with other peaks prevents unambiguous NOE assignments in this region.

Although the folding intermediate of the WT FF domain from HYPA/FBP11 forms rapidly (on the microsecond–timescale), the 3D structural model of the I state shows that its rearrangement to the native conformation can only occur through the breaking of non-native secondary and tertiary interactions that slow the folding process by approximately two orders of magnitude. Non-native interactions along folding pathways that trap intermediate states may be more common than appreciated. The α-helical proteins Im7 (*4*), Rd-apocytb$_{562}$ (*45*), the R16 and R17 domains of α-spectrin (*46*), and EnHD (*47*) all fold via intermediates with non-native interactions that must be broken in a rate-limiting step before formation of native structures (*48*).

The methodology presented here for structural studies of invisible, transiently formed protein states is not restricted to folding intermediates but includes excited states important for function—for example, enzyme catalysis and ligand binding. As such, relaxation dispersion NMR spectroscopy holds great promise for providing important structural information on a large number of elusive conformers that play critical roles in a wide range of biochemical processes.

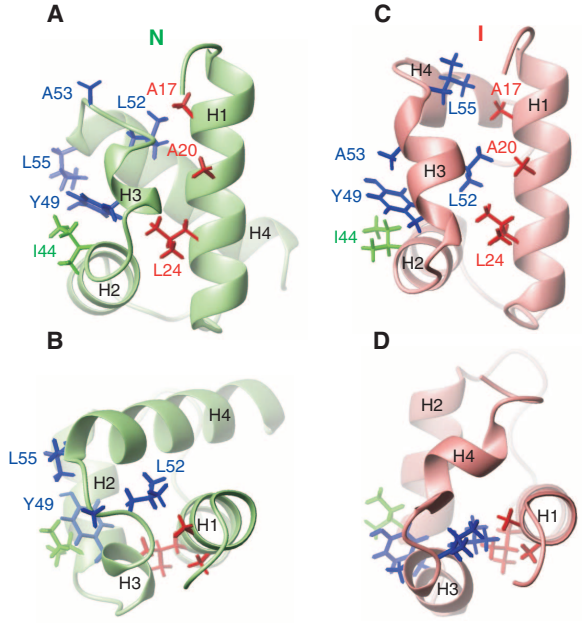

Fig. 4. Non-native interactions in the intermediate state. Structure and packing in the FF domain–folding intermediate [pink, (**C** and **D**)] as compared with the native protein [light green, (**A** and **B**); PDB code 1UZC (*20*)]. Side chains of residues from helices H1 (red), H2 (green), and H3 (blue) that form non-native contacts in the intermediate state are outlined. Structures on the bottom [(B) and (D)] are rotated by 90° relative to those on the top.

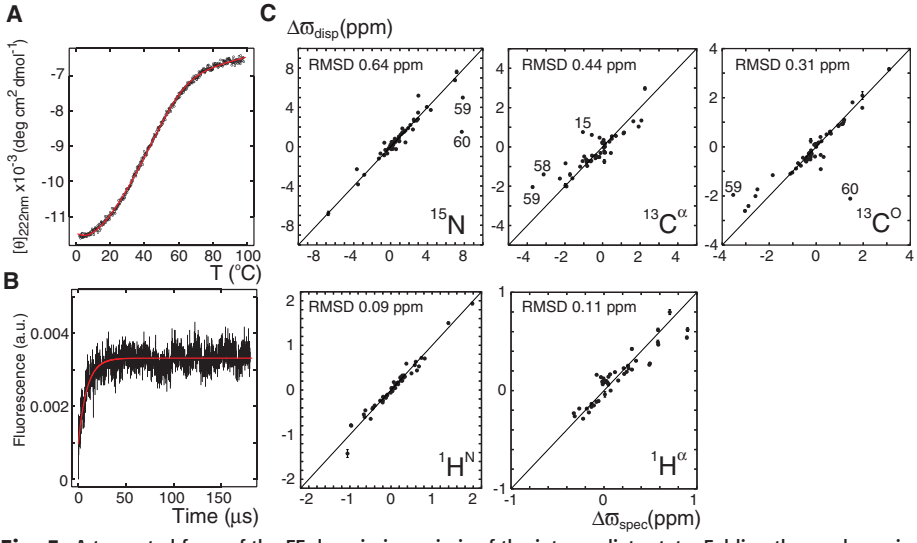

Fig. 5. A truncated form of the FF domain is a mimic of the intermediate state. Folding thermodynamics and kinetics of FF_{1-60} are characterized, respectively, by (**A**) thermal denaturation monitored by far ultraviolet circular dichroism (*41*) and (**B**) a laser-induced temperature jump (from 23° to 25°C) monitored by fluorescence (*23*, *42*). θ, ellipticity; T, temperature; a.u., arbitrary units. The red lines indicate fits to the experimental data (black). (**C**) Backbone ^{15}N, $^1H^N$, $^{13}C^\alpha$, $^1H^\alpha$, and $^{13}C^O$ chemical-shift differences between FF_{1-60} and FF_{1-71}, $\Delta\varpi_{spec}$, versus chemical shift differences between intermediate and native states (of FF_{1-71}), $\Delta\varpi_{disp}$, extracted from relaxation dispersion data. RMSD values between data sets calculated excluding points marked by residue numbers are shown in the top left corner of each plot. Resonance assignments for ^{15}N,^{13}C-labeled FF_{1-60} were obtained with the use of standard triple-resonance NMR experiments (*43*, *44*).

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52. We thank J. Forman-Kay (Hospital for Sick Children, Toronto) for providing laboratory space and useful discussions, P. Jemth (Uppsala Univ.) for providing plasmids for protein expression, R. Vernon (Univ. of Washington, Seattle) for valuable discussions, and R. Muhandiram (Univ. of Toronto) for NMR support. T.L.R. acknowledges the European Molecular Biology Organization (ALTF 827-2006) and the Canadian Institutes of Health Research (CIHR) for postdoctoral fellowships. L.E.K. holds a Canada Research Chair in Biochemistry. This work was supported by a grant from the CIHR to L.E.K. The structural ensembles of the WT FF domain–folding intermediate have been deposited in the Protein Data Bank (PDB; www.rcsb.org) with accession code 2KZG.

Supporting Online Material

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Materials and Methods
Figs. S1 and S2
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REPORTS

Electromechanical Computing at 500°C with Silicon Carbide

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Logic circuits capable of operating at high temperatures can alleviate expensive heat-sinking and thermal-management requirements of modern electronics and are enabling for advanced propulsion systems. Replacing existing complementary metal-oxide semiconductor field-effect transistors with silicon carbide (SiC) nanoelectromechanical system (NEMS) switches is a promising approach for low-power, high-performance logic operation at temperatures higher than 300°C, beyond the capability of conventional silicon technology. These switches are capable of achieving virtually zero off-state current, microwave operating frequencies, radiation hardness, and nanoscale dimensions. Here, we report a microfabricated electromechanical inverter with SiC complementary NEMS switches capable of operating at 500°C with ultralow leakage current.

High-temperature measurement and control instrumentation require microcontrollers, in addition to sensors and interface electronics, for a variety of important applications (such as automotive and aerospace propulsion systems, deep-well drilling, and geothermal exploration) in which the ambient temperature typically ranges from 300° to 600°C (*1*). However, limited by their band gaps, the mature silicon technologies [for example, a complementary metal-oxide semiconductor (CMOS)] are not applicable to this field due to excessive leakage caused by p-n junction degradation and thermoionic leakage (*2*). At these temperatures, thermally excited electrons in silicon can overcome the gate potential, and the intrinsic carriers excited by the thermal energy exceeds the amount of doped carriers. Thus, the electrical properties will be considerably influenced by thermally generated carriers, and the devices fail. To this end, wide–band-gap semiconductors like SiC have been of interest for these applications. Such materials, with adequate conductivity, offer a potential solution to expensive thermal-management and heat-sinking requirements, which pose a major barrier to continued shrinking of electronics. To date, the SiC electronic platform has been regarded as the most viable technology for high-temperature applications. Various field-effect transistor (FET) architectures have been considered as building blocks of this platform. Among alternative device architectures, the SiC junction field-effect transistor (JFET) is the most promising candidate for high-temperature logic applications (*3*, *4*). Lack of good-quality gate insulator and low inversion-layer mobility have limited the development of SiC metal-oxide semiconductor FETs (*5*–*7*). On the other hand, Shottky-based metal semiconductor FETs exhibit notable gate-to-channel leakage at elevated temperatures (*8*). As a depletion-mode device, the JFET

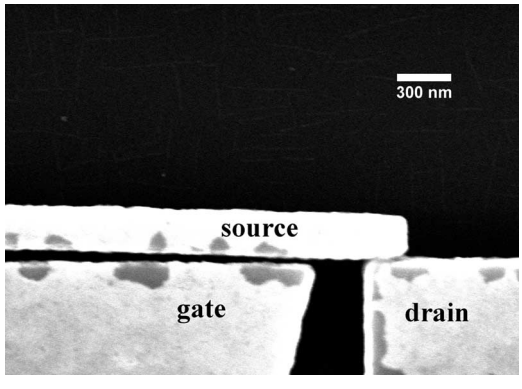

Fig. 1. A scanning electron micrograph showing the ON state of the three-terminal SiC NEMS switch. The spacing between the gate and drain is 300 nm. The initial actuation-gap height, defined as the distance between source and gate, is 150 nm without applying any potential. Lateral movement of the cantilever due to electrostatic attraction between the source and gate causes the beam to contact the drain. After the contact of source and drain, the gap between source and gate becomes only 25 nm.

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alleviates these problems. However, the large-size, high-threshold voltage, and low switching speed makes logic design with SiC JFETs unattractive. In addition, the wasted power caused by leakage current increases markedly with rising temperature. Replacing existing SiC JFETs with nanoelectromechanical system (NEMS) switches is an attractive alternative for low-power, high-performance logic operation (*9*–*11*) at high temperatures. These switches can achieve virtually zero off-state current (that is, almost no leakage current), can be fabricated at nanoscale dimensions, and can operate at microwave frequencies (up to 1 GHz) (*12*–*14*). The excellent thermal stability, chemical inertness, and mechanical robustness make SiC a suitable material for this technology. High-temperature packaging is usually a challenge (*15*); it is accomplished with the use of ceramic (e.g., Al_2O_3 and AlN) packages incorporating gold-wire bonding (*16*, *17*). For example, high-temperature packaging for a SiC pressure sensor has been demonstrated by Chen and Mehregany for in-cylinder pressure monitoring (*18*). In addition, thousands of operation hours of SiC JFETs at 500°C using Al_2O_3 package substrate and gold bonding wire has been demonstrated by Neudeck *et al.* (*3*). Here, we report the microfabrication of an electromechanical inverter using SiC complementary NEMS switches that operates at 500°C with ultralow leakage current (four orders of magnitude less than SiC JFETs). This logic element, which is also radiation tolerant, presents a technology basis for all-mechanical computation at high operational temperatures.

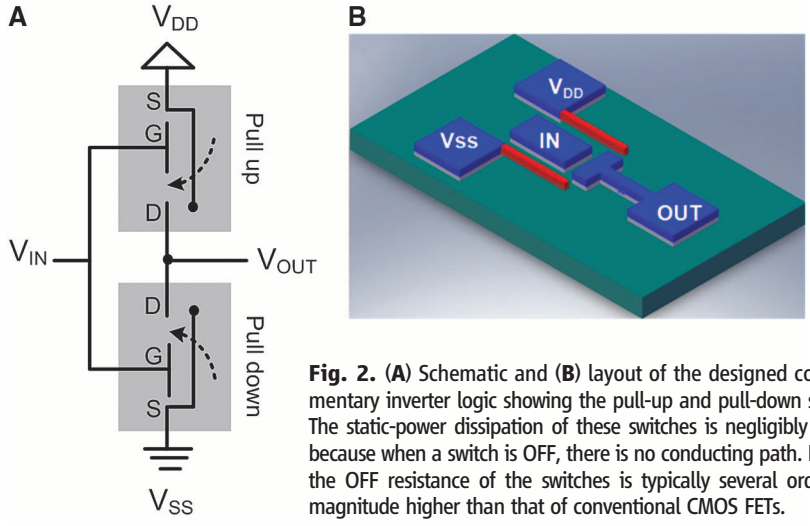


Fig. 2. (**A**) Schematic and (**B**) layout of the designed complementary inverter logic showing the pull-up and pull-down stages. The static-power dissipation of these switches is negligibly small, because when a switch is OFF, there is no conducting path. Hence, the OFF resistance of the switches is typically several orders of magnitude higher than that of conventional CMOS FETs.

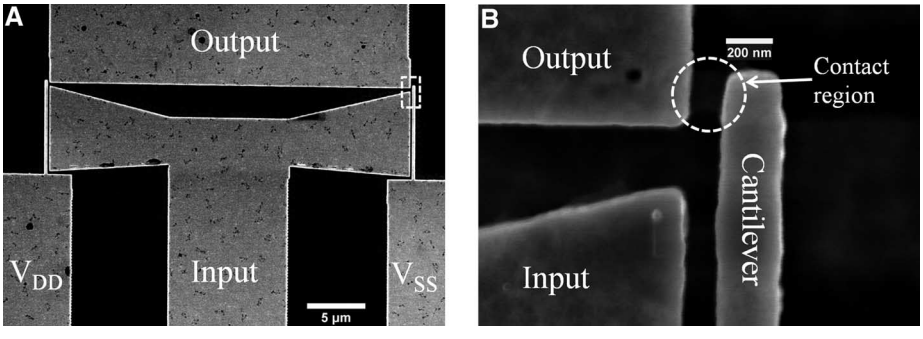
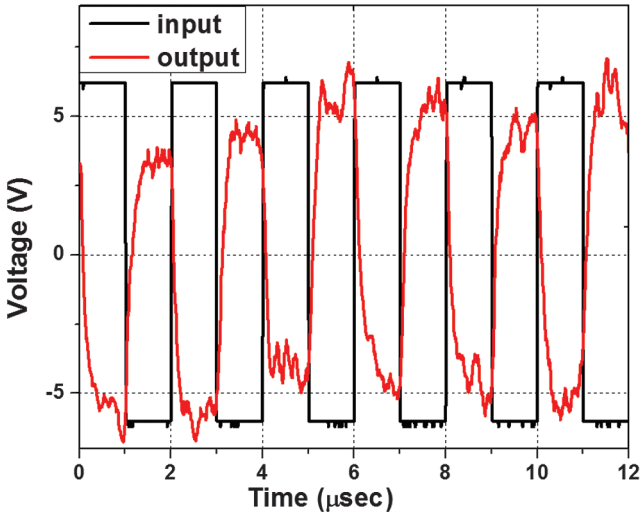


Fig. 3. Scanning electron micrographs of (**A**) a fabricated inverter with (**B**) a magnified picture highlighted in (A) showing the cantilever connected to V_{SS} and the corresponding actuation gap.

Fig. 4. Input-output voltage waveform of the inverter at 500°C. The output voltage maintains inverting behavior, although the voltage swing shows slight degradation.



The electromechanical inverter is designed using two laterally actuated NEMS switches following a complementary static-CMOS logic style (*19*), which consists of pull-up and pull-down stages. Each switch has three terminals: source (S), gate (G), and drain (D), where the gate is used as a control terminal to create a conducting path between the drain and source through electrostatic actuation. As shown in Fig. 1, the ON state of the switch is represented by the contact of the S and D to form the conducting "channel." Figure 2A shows the schematic of the inverter. This logic style was chosen because it provides low noise sensitivity and low static-power consumption.

The fabricated SiC inverters (Fig. 3) consist of two identical three-terminal switches; the length, width, and actuation gap of the cantilevers are ~8, ~200, and 150 nm, respectively. A 100-mm-diameter (100) Si wafer with a 500-nm-thick thermally grown silicon dioxide layer is used as the substrate. Heavily nitrogen-doped ($N_D \sim 1 \times 10^{20}$ cm^{-3}) polycrystalline 3C-SiC films are deposited on the wafer by low-pressure chemical-vapor deposition to a thickness of 400 nm (*20*). Next, a 40-nm-thick Ni etching mask layer is deposited by thermal evaporation and patterned by electron-beam lithography and lift-off. The Ni etch mask pattern is then transferred to the SiC film by deep reactive-ion etching with SF_6 as etch gas. HF wet etching removes the sacrificial silicon dioxide layer, followed by carbon dioxide critical point drying to suspend the patterned SiC beams above the Si substrate.

The two laterally actuated cantilevers of the inverter are connected to positive- (V_{DD}) and negative-voltage (V_{SS}) terminals, respectively. When applying a positive input (logic high), the electrostatic force between the input and the cantilever connected to V_{SS} overcomes the restoring force of the beam, and the cantilever moves laterally to contact the output, providing a logic low. A logic high can be obtained by supplying a negative input to actuate the beam connected to V_{DD}. Due to the complementary nature of the logic, the output terminal (V_{OUT}) is connected to either V_{DD} (for logic "0" at the input terminal V_{IN}) or V_{SS} (for logic "1" at V_{IN}), but not both, thus preventing any direct current path at the steady state. Switches have been verified to work at 500°C in air. However, to prevent surface oxidation, we conducted high-temperature testing in a nitrogen environment

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using a resistive heater, with the devices packaged in ceramic dips. Field applications would make use of a vacuum package, which also prevents surface oxidation and additionally eliminates viscous drag forces during switch operation.

Inverter operation has been demonstrated at 500°C (Fig. 4) with V_{DD} = 6 V and V_{SS} = –6 V, at an operating speed of 500 kHz. The logic level is clearly higher than the existing Si logic devices, which operate at 3 V or lower. However, the threshold voltage of the fabricated switches is compatible to other competing high-temperature electronics (*3*, *4*). The logic level can be further reduced by narrowing the actuation gap (*21*) as the nanofabrication technology advances. NEMS switches based on carbon nanotubes exhibiting a threshold voltage smaller than 4 V have been demonstrated with gaps smaller than 100 nm (*22*, *23*). In theory, the actuation voltage of the NEMS switches can be scaled beyond the threshold voltage of CMOS, whose scaling is limited by the thermal voltage k_BT/q (here, k_B is the Boltzmann constant, T is temperature, and q is the charge of an electron). The active area of the demonstrated inverter consisting of two complementary NEMS switches is ~8 μm^2, excluding connecting traces and contact pads. Compared to modern (90-nm gate length) nanoscale Si CMOS logic devices, which have a standard-cell inverter gate with a minimum active area of ~0.1 μm^2 (*24*), the presented device is much larger. However, this demonstrated inverter is already about three orders of magnitude smaller than most reported high–temperature, JFET-based logic gates, which have gate lengths ranging from tens to few hundreds of microns (*3*, *4*). With improvement in nanolithography, it appears very plausible to scale the dimensions of the NEMS switches to achieve higher integration density, along with lower operating voltage and higher switching speed.

Typical switches have operated ≥21 billion cycles at 25°C and ≥2 billion cycles at 500°C; the measured leakage current at the OFF state is less than 10 fA (below the noise floor of the measuring tool). Failure at 25°C is breakage of the switching cantilever beam at the location of highest stress, characterized by a clean fracture. However, at 500°C, the broken cantilever beam has a ball of SiC at one side of the fracture gap that is likely to be local melting—an unexpected event because SiC sublimates at 1800°C. Thus, the mechanism for the high-temperature failure is not yet understood. Overall, this achievement of a SiC NEMS-based inverter operating at 500°C creates a pathway toward energy-efficient high-temperature computation.

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Supporting Online Material

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A Red-Shifted Chlorophyll

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Chlorophylls are essential for light-harvesting and energy transduction in photosynthesis. Four chemically distinct varieties have been known for the past 60 years. Here we report isolation of a fifth, which we designate chlorophyll f. Its in vitro absorption (706 nanometers) and fluorescence (722 nanometers) maxima are red-shifted compared to all other chlorophylls from oxygenic phototrophs. On the basis of the optical, mass, and nuclear magnetic resonance spectra, we propose that chlorophyll f is [2-formyl]-chlorophyll a ($C_{55}H_{70}O_6N_4Mg$). This finding suggests that oxygenic photosynthesis can be extended further into the infrared region and may open associated bioenergy applications.

Chlorophylls (Chls) are the essential pigments of photosynthesis, for which they both harvest light and transduce it into chemical energy. There are four chemically distinct chlorophylls known to date in oxygenic photosynthetic organisms, termed Chls a, b, c, and d in the order of their discovery (*1*, *2*). All four pigments are present in light-harvesting complexes, though until recently only Chl a was thought to be indispensable for energy transduction in the photosystem reaction centers (*3*). This paradigm was challenged when Chl d, long considered an artifact since its discovery in 1943 (*4*), was shown to constitute up to 99% of all Chl in the cyanobacterium *Acaryochloris marina* (*5*). In this and related organisms, Chl d can replace Chl a in the photosystems of oxygenic photosynthesis, thereby extending to the red the spectrum of light that can be harvested for carbon fixation (*6*). Here we report yet another chlorophyll, which we designate Chl f (*2*), that absorbs even further to the red.

The morphological features of stromatolites provide a unique environment for specific but diverse cyanobacterial communities (*7*). We cultured a sample from Hamelin pool under near-infrared light (720 nm) (*8*). Analysis of a methanolic extract of stromatolites from Shark Bay, Western Australia, by high-performance liquid chromatography (HPLC) revealed a complex mixture of chlorophylls (Fig. 1A): In addition to a detectable amount of Chl a (peak 3) and bacteriochlorophyll a (peak B), there were trace amounts of Chl d and a new pigment, Chl f (peak 2 in Fig. 1A). The optical absorption spectrum of Chl f in neat methanol has a red-shifted Q_Y transition [wavelength of maximum absorption (λ_{max}) = 706 nm] compared to other chlorophylls and a blue-shifted Soret band (λ_{max} = 406 nm) (Fig. 1, B and D). The room-temperature fluorescence emission of isolated Chl f is maximal at 722 nm (with excitation wavelength of 407 nm) (Fig. 1D), which is also considerably red-shifted compared to other Chls (*9*). Chlorophyll f appears to be made by a filamentous cyanobacterium (fig. S3) based on the 16*S* ribosomal RNA (rRNA) sequence of our purest enrichment III culture (see supporting text), which contained only Chl a and Chl f by HPLC analysis.

We assigned the molecular formula of Chl f ($C_{55}H_{70}O_6N_4Mg$) by mass spectral analysis based on the molecular ion at 906 *m/z* (mass/charge ratio). Phytol ($C_{20}H_{38}$) was identified by the prominent fragment at 628 *m/z* (fig. S1B), and Mg as the central metal by the molecular ion of the pheophytin (Pheo) (884 *m/z*, $C_{55}H_{72}O_6N_4$). A

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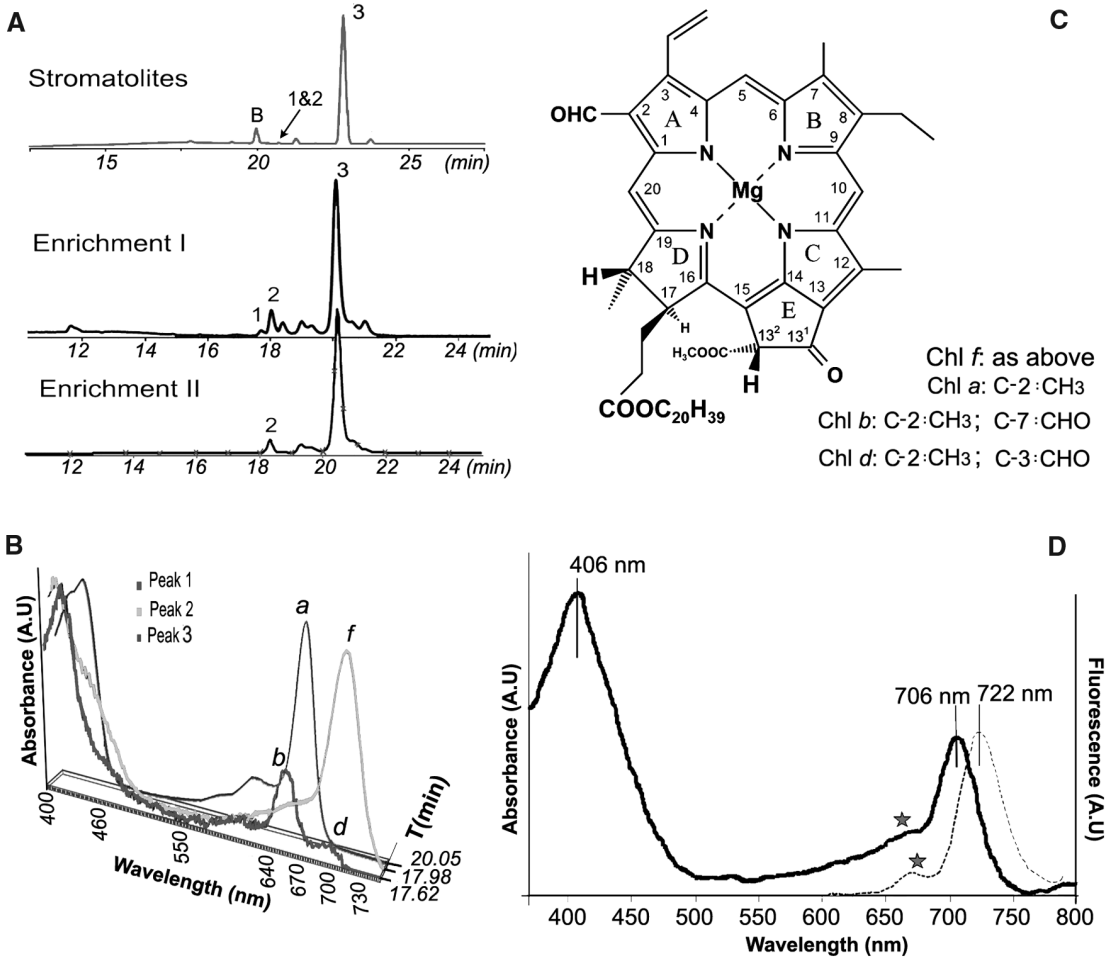

Fig. 1. (**A**) HPLC traces detected on the basis of Q_Y absorbance (600 to 750 nm) of methanolic extracts from the stromatolite sample and from aerobic enrichment cultures I and II (see supporting material). Differences in retention times between the top and the two lower traces are due to different chromatographic solvent systems (CH_3CN·CH_3OH to CH_3OH gradient above, CH_3OH·H_2O to CH_3OH gradient below). (**B**) Spectral comparison of HPLC peaks of interest from enrichment culture I: peak 1 (retention time t_r = 17.62 min) contains Chl b and Chl d, peak 2 (t_r = 17.98 min) mainly Chl f characterized by its red-shifted Qy absorption band (706 nm), and peak 3 (t_r = 20.05 min) Chl a. (**C**) Chemical structure of Chl f with comparison to other chlorophylls. (**D**) Absorbance and fluorescence emission spectra (λ_{exc} = 407 nm) of purified Chl f in methanol at room temperature. Contributions from a Chl a–like contaminant are indicated by stars.

formyl group was identified by ^{1}H nuclear magnetic resonance (NMR) spectroscopy of Chl f [δ = 11.35 ppm (parts per million)] (fig. S2); the red-shifted Q_Y optical transition (Fig. 1D) suggested substitution on rings A or C (Fig. 1C). The transformation of a methyl to a formyl moiety is a known modification of Chl a, producing Chl b (*10*). Because Chl d has a formyl group at C-3 (*3*), and differs in its properties, this leaves C-2 and C-12 as potential sites that comply with the mass spectrum. Substitution at C-2 is implicated by the methine pattern of the NMR spectrum (fig. S2): No methine resonates at δ > 10 ppm, which would be the expected chemical shift for the 10-H in the event of a neighboring 12-CHO group (*11*); moreover, the clustering of the C-5, C-10, and C-20 methine resonances at 9.86, 9.79, and 9.77 ppm is expected for C-2 substitution based on the known spectra of Chls a, b, and d and spectra simulated by density functional theory (DFT) (table S1). Substitution at C-2 is also supported by DFT calculations of the optical spectra, which predict a large red-shift of the Q_Y band relative to Chl a for a 2-CHO group ($\Delta\lambda$ = 37.6 nm), and, surprisingly, a blue-shift for a 12-CHO group ($\Delta\lambda$ = −6.5 nm) (table S2). Therefore, we propose that Chl f is [2-formyl]-Chl a (Fig. 1C). Isolation of cultivable pure strains bearing Chl f will be essential to define the function of this intriguing chromophore.

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Coherence Resonance in a Single-Walled Carbon Nanotube Ion Channel

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Biological ion channels are able to generate coherent and oscillatory signals from intrinsically noisy and stochastic components for ultrasensitive discrimination with the use of stochastic resonance, a concept not yet demonstrated in human-made analogs. We show that a single-walled carbon nanotube demonstrates oscillations in electroosmotic current through its interior at specific ranges of electric field that are the signatures of coherence resonance. Stochastic pore blocking is observed when individual cations partition into the nanotube obstructing an otherwise stable proton current. The observed oscillations occur because of coupling between pore blocking and a proton-diffusion limitation at the pore mouth. The result illustrates how simple ionic transport can generate coherent waveforms within an inherently noisy environment and points to new types of nanoreactors, sensors, and nanofluidic channels based on this platform.

Stochastic resonance (*1*, *2*) as a detection mechanism occurs when a subthreshold signal is amplified instead of obscured by environmental noise, allowing for discrimination despite stochastic interference. There are many examples of this in biological systems, including crayfish detecting incident pressure waves from predators (*3*), plankton detection by paddlefish (*4*), the cercal sensory system of crickets (*5*), and human visual perception (*6*) and balance control (*7*). The distinguishing attribute of these systems is that the signal-to-noise ratio of the sensory output increases to an optimum value with increasing noise, the signature of stochastic resonance. In 1995, Bezrukov and Vodyanoy (*8*) reported that a collection of alamethicin ion channels constituted the simplest experimental system capable of stochastic signal enhancement. It still remains an open experimental question whether a single, static ion channel alone can demonstrate this important function (*9*), or if stochastic resonance can be reliably incorporated into human-made devices. A synthetic ion channel with no complexity associated with multiple proteins and their conformational states may help to resolve this question. A nanopore formed from the interior of a single-walled carbon nanotube (SWNT) has captivated the interest of many theorists, who have predicted enhanced water permeation (*10*), large proton fluxes (*11*), icelike water phases (*12*), and high ion-rejection rates (*13*). However, it has proven difficult to experimentally observe the translocation of individual small ions, such as Na^+ and K^+, from a single isolated nanotube, despite success with macroscopic ensembles forming various membranes for gas and liquid separations (*14*, *15*). We studied transport of single ions through the interior of a single 500-μm-long carbon nanotube and observed a proton flux of ~10^8 protons/s. This nanopore system can show oscillations in the electroosmotic current at constant bias, resulting in rhythmic, mode-locked frequencies of ion transport that arise from coherence resonance, a variant of stochastic resonance characterized by self-synchronization at an optimal noise level. This resonant transport substantially increases the throughput of a nanopore by a factor of 100. Liu *et al.* (*16*) recently designed a SWNT nanopore for DNA translocation using a much shorter length (2 μm) and higher electric field (~10^5 V/m), but they did not observe stochastic pore blocking, particularly from ions. Our results show that simple, single-ion transport from an isolated nanopore is all that is needed to produce a stochastic resonant mechanism, and they also open the door to new types of chemical nanoreactors, nanofluidic conduits, and single-molecule sensors.

We created the SWNT ion channels (diameter 1.3 to 2.3 nm, average 1.5 nm) with the use of an epoxy structure (Fig. 1) with two compartments bonded onto a Si/SiO_2 wafer containing an array of chemical vapor deposition (CVD)–synthesized, ultralong aligned SWNTs (*17*). After filling with various aqueous ionic solutions (NaCl, LiCl, or KCl), we monitored the ion current with Ag/AgCl electrodes in either well and standard voltage-clamp techniques (*18*). We measured current traces for various applied electric fields (600 to 6000 V/m) across reservoirs connected by up to 45 nanotubes that are 500 μm long (Fig. 2A). We observed stochastic fluctuations in the ion current that are quantized, similar to observations of biological ion channels (*19*) and solid-state nanopores (*20*) as signatures of stochastic pore blocking.

The step height, or the current decrease (ΔI), is the amount of reduced flux of charge-carrying species upon pore blocking. The velocity and, thus, the mobility of the blocker (in case the blocker translocates through the nanotube) can be estimated from the width of the downward peaks, or the dwell time, τ_{dwell}. Each peak in an all-point histogram (Fig. 2A, right) corresponds to a single

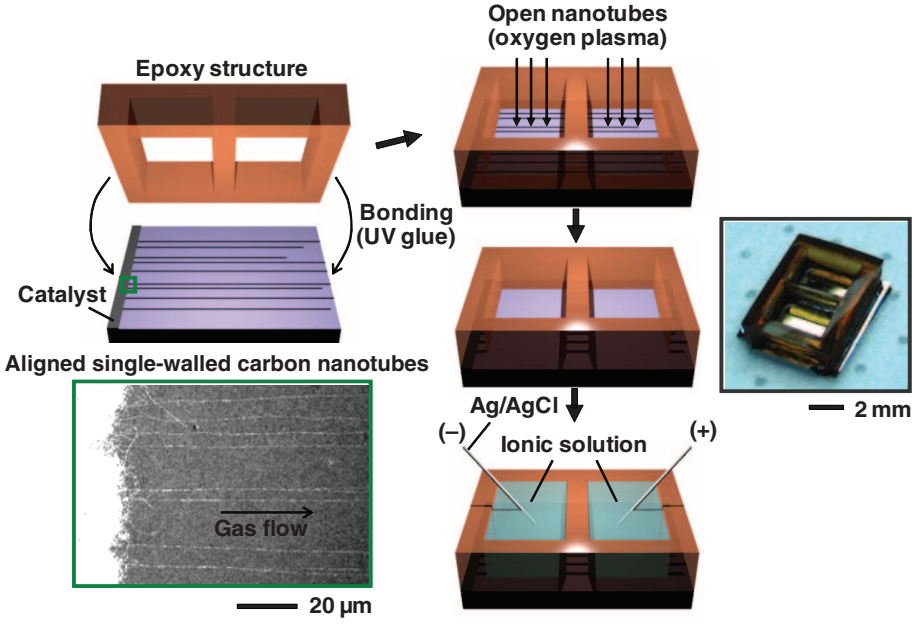

Fig. 1. Fabrication of SWNT ion channels. An epoxy structure with two compartments is bonded onto a substrate with ultralong and aligned CVD-grown nanotubes (scanning electron microscope image). Plasma etching removes the SWNT at the reservoir bottoms, opening both ends of nanotubes that span the divider between compartments. Both compartments are filled with ionic solution, and the electroosmotic current through the nanotubes is monitored. The epoxy structure serves as a mask during plasma etching and as an efficient inhibitor of exterior transport along the nanotube (figs. S4 to S6). UV, ultraviolet.

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pore state. The presence of three major states in the top trace in Fig. 2A suggests that the events are from two nanotubes. We note that there is a threshold voltage that must be exceeded for pore-blocking events to be observed. For each sample, there is an optimal voltage to observe blocking events, and we tune to this region with each experiment. By carefully adjusting the bias to the low field threshold of this region, we could regularly observe current fluctuations between only two states with conserved ΔI (remaining Fig. 2A traces), indicative of the single-tube phenomenon (*21*). The inactive nanotubes in the system are either permanently blocked by impurities or remain below the requisite field to clear low-mobility blocking species within the observation window of the experiment. In this way, transport across a single nanotube can be studied, as indicated by the observation of a two-state Coulter effect. This two-state stochastic blocking phenomenon is evidence of single-molecule transport in a singular, isolated channel across a diverse range of fields: from patch clamp experiments on biological ion channels (*19*) to synthetic nanopores (*20*).

A series of control and comparison experiments reveal that the dominant ion conductor consists of protons, with cations from the added electrolyte as the dominant blocking species. First, the unblocked current levels decrease with an increase in salt concentration (fig. S7), which is consistent with previous reports of highly unfavorable K^+ or Cl^- partitioning into the interior of an uncharged nanotube (*13*, *15*). Hence, only H^+ and/or OH^- may be the majority charge carriers. Several theoretical studies indicate that proton conduction along the hydrogen-bonded water network inside the SWNT should be faster than in bulk water (*11*). The proton conduction can occur via a "hop-and-turn" Grotthuss mechanism along the water chain (*22*) and does not require physical translocation of protons. The current levels are enhanced by the addition of HCl (1 M) and only upon addition to the anode (+) (fig. S8). Higher conductance change upon pore blocking (ΔG) at acidic pH further supports our claim (fig. S9). Conversely, Fig. 2 shows that the blocking events change markedly with the type and concentration of added electrolyte, with the cation appearing to be the dominant blocker. We fed cations of successively larger hydration radius (with the anion unchanged as Cl^-) to the nanotube ion channel and found that 1 M tetramethylammonium (TMA) chloride [crystallographic diameter of TMA^+ ~ 0.7 nm (*23*)] yielded no blocking events (fig. S10), even though Cl^- should be small enough to translocate. The etched ends of nanotubes from the oxygen plasma bear carboxylic acid groups with pK_a of ~4.5 (where K_a is the acid dissociation constant) (*24*). The repulsion of anions is consistent with these observations. Impurities and other artifacts are also readily ruled out (*25*–*28*).

The SWNT proton channels demonstrate unusually high conductivity compared with sputtered Si ion channels (*29*), which are typically ~10^4 times less conductive for KCl, even at larger diameters. The difference highlights the contribution of the hydrogen-bonded water network (*12*) in the former that contributes substantially to proton conduction. The typical current blocking of 100 pA corresponds to 6.25×10^8 protons/s. This value is comparable to the maximum rate reported from water-filled gramicidin proton channels (2.2×10^9 protons/s) under strongly acidic conditions (*30*). The result suggests highly efficient proton conduction through SWNT, enhanced by the expected accumulation of protons near the negatively charged pore mouth (*30*). The high aspect ratio of our nanochannel (>250,000) appears critical for the detection of single ions in aqueous solution. Despite some similarities with biological ion channels, the transport mechanisms in the nanotube are distinct in that they do not conduct or gate ions by conformational changes in pore structure (*31*).

The necessity of partially shedding hydration shells imposes an energetic threshold on ions entering a nanochannel (*13*). In protein ion channels this barrier is minimized by carbonyl oxygen mimicking the hydration environment (*32*), whereas in carbon nanotubes, the activation energy must be supplied externally. The observed minimum threshold voltage of 100 mV in our study falls into

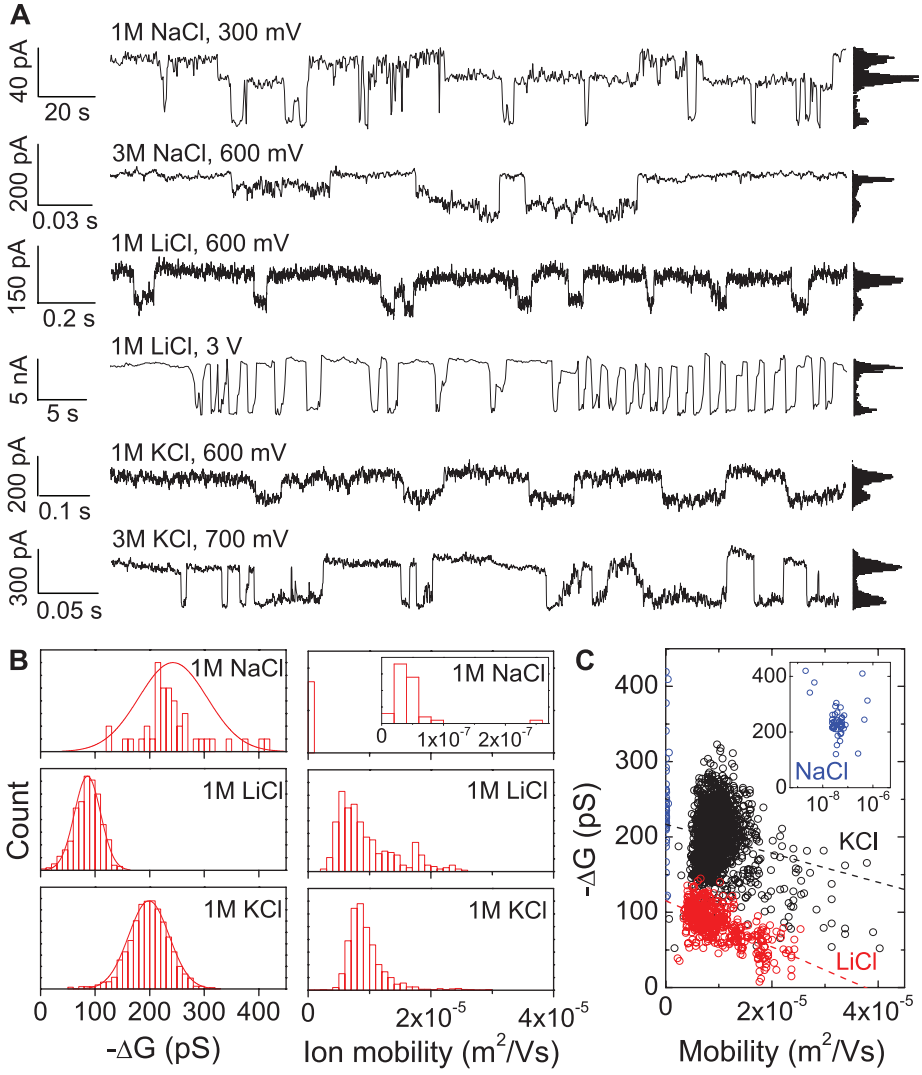

Fig. 2. Detection of individual cation transport through the interior of a single nanotube. (**A**) Stochastic blockage and recovery of the proton flux through the SWNT interior is observed at varied electric fields and with different ion types. Several control experiments reveal that cations in NaCl, LiCl, and KCl are the pore blockers. The top trace (1 M NaCl, 300 mV) shows three distinct pore states as indicated in three peaks in an all-point histogram (right), suggesting that the blocking events are from two nanotubes. Careful adjustment of the bias results in transitions observed between only two states (second trace and all others) and allows for the study of the single-tube phenomenon. (**B**) Histograms of the conductance decrease upon pore blocking, ΔG (left), and ion mobility (right) for the tested ions. Proton conductivity, estimated from ΔG = 200 pS and assuming a tube diameter of 1.5 nm, is 5×10^2 S/cm. The ion mobility is 100 times higher than the value in bulk water. (**C**) The conductance change with blocking, ΔG, decreases with ion mobility, as expected. (Inset) Small mobility region is zoomed in for NaCl.

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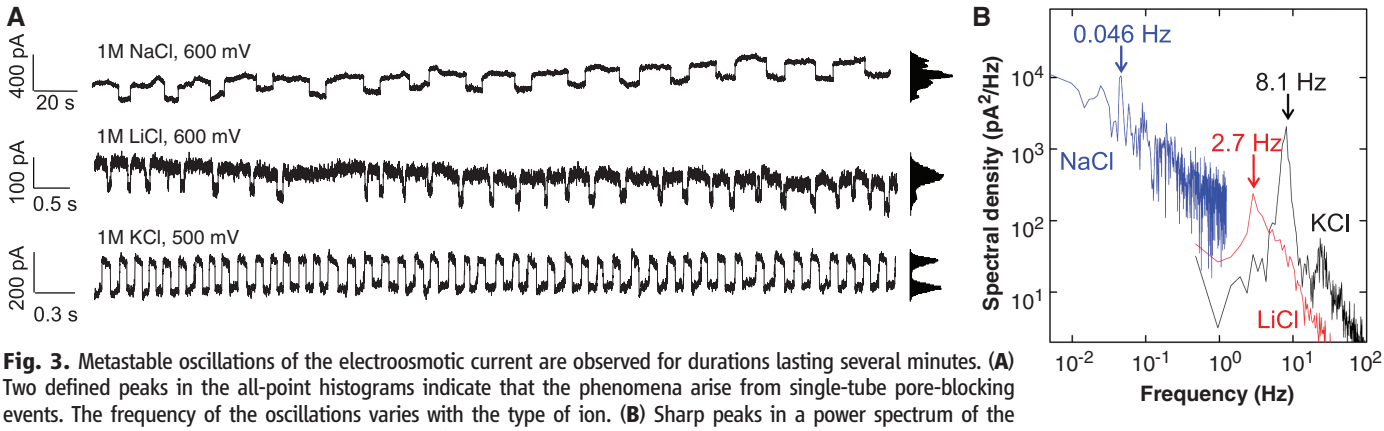

Fig. 3. Metastable oscillations of the electroosmotic current are observed for durations lasting several minutes. (**A**) Two defined peaks in the all-point histograms indicate that the phenomena arise from single-tube pore-blocking events. The frequency of the oscillations varies with the type of ion. (**B**) Sharp peaks in a power spectrum of the electroosmotic current are pronounced at the oscillation frequencies.

the range of theoretically predicted free energy of permeation: 80 to 150 meV (*13*). Ensemble measurement by Fornasiero *et al.* (*15*) reported the percentage of ion rejection by a nanotube membrane at varied ion concentration and valence; the rejection of anions was more efficient because the pore mouth was negatively charged. The ability of our system to count single ions allows precise measurement of the separation factor (proton rate/alkali cation rate). The complete rejection of ions can be achieved below the threshold, and the minimum separation factor at suprathreshold voltage is as high as 6×10^7. This high rejection rate reinforces the notion that membranes based on carbon nanotubes may have applications to desalination of sea water and water purification.

The blocking events provide information about hydrated-ion transport in the carbon nanotube, a subject of intense theoretical investigation (*13*, *33*). The histograms (Fig. 2B) of the blocking currents (ΔG) show Gaussian distributions for Li^+ and K^+ (with too few events for Na^+) and mean values that scale as $Na^+ > K^+ > Li^+$. The ratio of the areas between the hydrated-ion cross section and that of the nanopore provides an estimate of the conductance change upon ion partitioning, ΔG, relative to the value at complete blockage, ΔG_{max}

$$\Delta G = \left(\frac{d_{ion}}{d_{tube} - \sigma_{C\text{-}O}}\right)^2 \Delta G_{max} \qquad (1)$$

Here, d_{ion} is the ion diameter; d_{tube} is the diameter of the nanotube, and $\sigma_{C\text{-}O}$ is the Lennard-Jones parameter for C-O interaction (0.0319 nm) (*10*). For example, K^+ produces ΔG values that vary between 52 and 323 pS (with the latter value taken as ΔG_{max}); therefore, d_{ion}/d_{tube} varies between 0.39 and 0.98, assuming $d_{tube} = 1.5$ nm. For Li^+, the ΔG range is 7.5 to 145 pS, and d_{ion}/d_{tube} is 0.22 to 0.98; for Na^+, ΔG is 120 to 420 pS, and d_{ion}/d_{tube} is 0.52 to 0.98. The ΔG value is smallest for the Li^+ ion, which has the smallest crystallographic diameter and the largest hydrated diameter in bulk. It is expected that $\Delta G_{Na^+} > \Delta G_{K+}$, due to stronger hydration around Na^+, which generally requires larger pore size as observed in protein ion channels (*34*), although Carrillo-Tripp *et al.* (*35*) predict higher hydration numbers for K^+. A rigid, synthetic nanopore capable of single-ion detection, as introduced in this work, may resolve outstanding questions about ion-hydration numbers in a confined space (*36*).

This ordering of the blocking currents is also consistent with the data shown in the mobility histograms in Fig. 2B, which should instead scale inversely with d_{ion}/d_{tube}. Here the Na^+ mean (5×10^{-8} m^2/Vs) is much smaller than that of Li^+ and K^+ with values of 8×10^{-6} m^2/Vs. The Gaussian distribution of τ_{dwell} leads to asymmetry in the mobility distribution (mobility ~ $1/\tau_{dwell}$). The smallest ΔG values accompany a large variation in mobility for Li^+, which has a small ionic diameter (0.12 nm). However, the mobility of Na^+ is nearly three orders of magnitude smaller by comparison, suggesting sterically hindered transport inside the nanotube. The values are two orders of magnitude higher than the cation mobility of bulk water and the theoretical mobility through a 3-nm-diameter SWNT (*37*) (both ~10^{-8} m^2/Vs). Theoretical treatments describe this high ion mobility as arising from the atomically smooth surface of the SWNT interior and velocity slip at the wall (*10*). Plotting ΔG versus mobility at 1 M (Fig. 2C) reveals an inverse relation, as expected for Li^+ (red) and K^+ (black), and describes the mean value of Na^+ (blue).

In some instances, we observed durations in which the cation-blocking events developed highly synchronized, rhythmic patterns (three of which are shown for each ion type in Fig. 3A). From the all-point histograms, it is clear that these oscillations occur from single-nanotube transport. A power spectrum from fast Fourier transform (FFT) of the resulting current output (Fig. 3B) reveals the oscillator frequencies as 0.046 Hz for NaCl, 2.7 Hz for LiCl, and 8.1 Hz for KCl. These instances appeared to be metastable and particularly sensitive to environmental perturbation, but otherwise could be observed for durations lasting several minutes (figs. S11 to S15). Despite extensive work examining synthetic analogs of the ion channels, sustainable current oscillation (*28*, *38*) produced from transport of single ions has not been observed. The productivity of the nanopore in terms of single-molecule processing dramatically increases during these periods, counting hundreds of individual cations per minute.

These oscillations are caused by a coupling between the stochastic pore blocking and a proton-diffusion limitation that develops at the pore mouth (Fig. 4A). The calculated proton mobility through the nanotube was substantially greater than that of the bulk solution [supporting online material (SOM) text]. Thus, an unobstructed proton current in the nanotube will necessarily deplete the proton concentration at the pore mouth. Coupling occurs because the depletion increases the relative blocking-ion concentration, thus increasing its probability of partitioning into the nanotube, an extremely rare event otherwise. Once the nanotube is blocked, the proton concentration at the pore mouth increases rapidly while the blocking cation traverses the nanotube. When the blocker emerges from the other side, the proton current is restored, and a subsequent blocking event is suppressed by the initially high concentration of protons relative to blocking cations. Reformation of the diffusion limitation as the proton flow is restored then allows this cycle to repeat indefinitely. We constructed a stochastic simulation (*39*) (Fig. 4B) with six equations and rate constants [diffusion of H^+ into (k_s) and out of (k_{sd}) the pore mouth region, partitioning of H^+ (k_1) and blocking cation (k_2) into the nanotube, and the exit of these two species from the nanotube (k_{1d} and k_{2d} for H^+ and blocker, respectively)] (SOM text) with a Gaussian dwell-time distribution known from our experiments. The blocking rate constant (k_2) is small compared with the proton value (k_1). This system reconstructs the oscillation frequencies observed experimentally for certain values of the proton-exchange rate constant (k_s) and also the Gaussian distribution in open-channel lifetime (τ_{open}) observed during the oscillations events in Fig. 3A.

The signature of stochastic resonance is one where the signal-to-noise ratio of the system maximizes at the optimal level of noise or random

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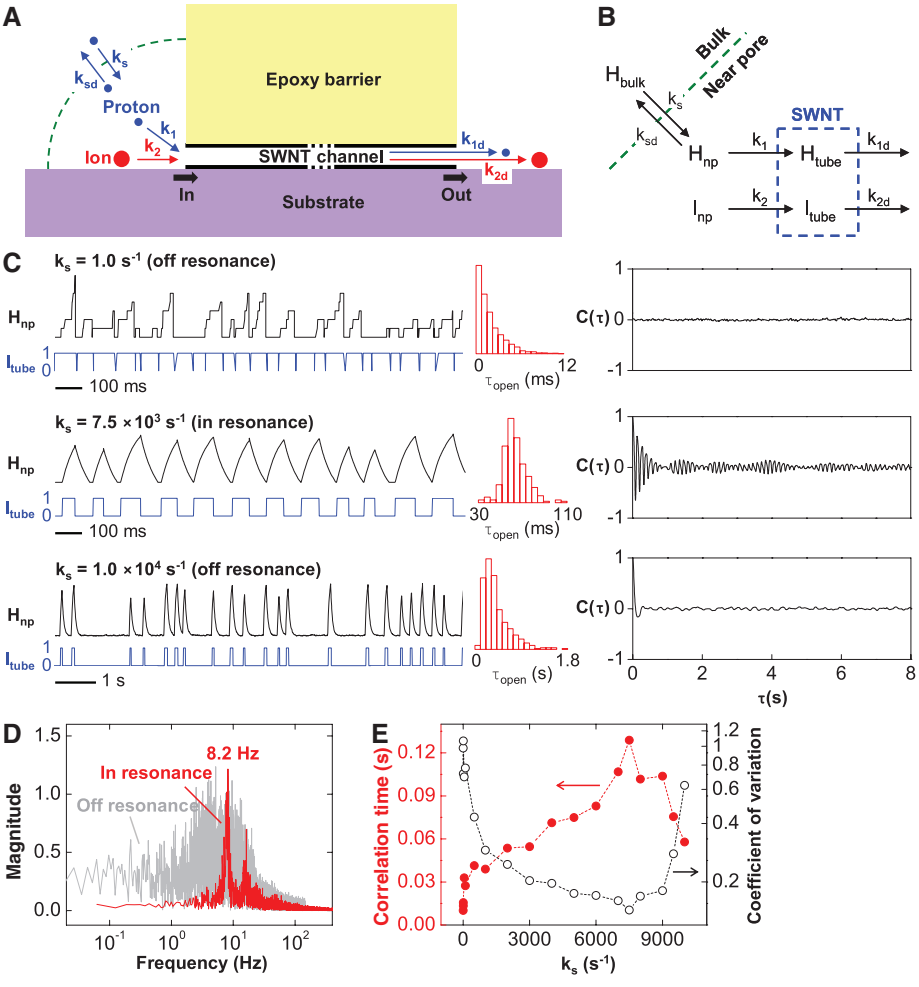

Fig. 4. Stochastic simulation illustrating the influence of coherence resonance on the oscillatory behavior. (**A**) Six reaction steps define this system: protons and blocking cations entering and transporting across the channel, as well as proton exchange between bulk and pore-mouth region. (**B**) Summary of the six reactions. (**C**) Trace of the number of protons at near-pore region (H_{np}, black) and ion occupancy in the nanotube (I_{tube}, blue) at varied rate constants of proton-in to near-pore (k_s). Histograms of open-channel lifetimes, τ_{open} (red), show Gaussian distributions at only optimal values of k_s (in resonance) and random, exponential distributions at larger and smaller values of k_s (off resonance). The autocorrelation function, $C(\tau)$, shown on the right is pronounced only when the system is in resonance. (**D**) Sharp peaks in the FFT appear only within the resonance window (red). (**E**) Characteristic correlation time (τ_C, red) and coefficient of variation (black) plotted versus k_s, a noise-defining parameter in our system, show that the optimal noise level exists for maximum characteristic correlation time or minimum coefficient of variation, corresponding to a maximum signal-to-noise ratio in the context of stochastic resonance.

fluctuations. In a typical demonstration, an external periodic forcing is superimposed with white Gaussian noise, with a resulting increase in the signal-to-noise ratio at an optimal noise level. In this work, the mechanism is best described by a coherence resonance (*40*), because the forcing function is intrinsic to the system dynamics. This phenomenon is illustrated in Fig. 4C by tuning the rate of proton diffusion into the near-pore region (k_s), which controls the inherent noise in the system. A value of k_s that is too large or too small to create the resonance condition results in a blocking frequency that is Poisson-like and erratic. As k_s approaches an inherent resonance condition, the distribution of the open-channel lifetime becomes Gaussian and narrow, and the blocking events occur with a locked frequency. This mathematical system can reproduce the frequency values of the oscillations (Fig. 4D) by examining the FFT of the blocking-cation occupancy.

For a quantitative description of coherence resonance in this mechanism, we calculate a characteristic correlation time, τ_C, from the normalized autocorrelation function, $C(\tau)$ (*40*)

$$\tau_C = \int_0^\infty C^2(\tau)d\tau, \quad \text{where}$$

$$C(\tau) = \frac{\langle \tilde{H}_{np}(t)\tilde{H}_{np}(t+\tau)\rangle}{\langle \tilde{H}_{np}{}^2(t)\rangle} \quad \text{and}$$

$$\tilde{H}_{np}(t) = H_{np}(t) - \langle H_{np}(t)\rangle \qquad (2)$$

Here, $C(\tau)$ represents the expected value of the product of number of protons at the near-pore region (H_{np}) and time-shifted H_{np} and, therefore, becomes pronounced as the two are correlated in time and periodic. (In the above equation, $\tilde{H}_{np}$ is deviation from the average value of H_{np}, and t is time.) τ_C at resonance corresponds to the interval between blocking events. Another measure of the coherence resonance is the coefficient of variation (*41*), defined in terms of the open-channel lifetime (τ_{open})

$$\text{Coefficient of variation} = \frac{\sqrt{\langle \tau_{open}{}^2\rangle - \langle \tau_{open}\rangle^2}}{\langle \tau_{open}\rangle} \qquad (3)$$

Both measures above are closely related to the signal-to-noise ratio (fig. S19). A summary of the coherence resonance appears in Fig. 4E, where the characteristic correlation time, as well as the coefficient of variation, is plotted versus k_s. There is an optimal rate of proton diffusion into the near pore (k_s) that maximizes the coherent signal and allows for oscillatory output.

The coherence-resonance condition dramatically increases the single-molecule processing rate of the nanotube (480 ions/min in resonance versus 5 ions/min off resonance). This result has implications for other nanopore systems, including DNA translocation and sequencing and Coulter detectors. The large proton conductivity opens possibilities for new types of proton-conducting membranes for fuel cells and catalysis. Our demonstration of single-ion detection in aqueous solution may allow for ultrasensitive detection technologies for environmental or biological monitoring of ion types differentiated by their dwell times. Our experimental system also provides an ionic resonator or waveform generator to the emerging family of devices that use ions for information processing, such as ionic transistors (*42*) and rectifier circuits (*43*). However, the ability to manipulate single small molecules (albeit, only ion manipulation is demonstrated in this work) may allow for the construction of chemical-reactor devices that process a single molecule at a time. The resonant transport condition necessarily ensures that only one molecule occupies the nanotube at any given time, which may be useful for manipulation and feedback control schemes, as well as coupling to external measurement devices for cataloging the single-molecule efflux.

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Ion-Mediated Electron Transfer in a Supramolecular Donor-Acceptor Ensemble

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Ion binding often mediates electron transfer in biological systems as a cofactor strategy, either as a promoter or as an inhibitor. However, it has rarely, if ever, been exploited for that purpose in synthetic host-guest assemblies. We report here that strong binding of specific anions (chloride, bromide, and methylsulfate but not tetrafluoroborate or hexafluorophosphate) to a tetrathiafulvalene calix[4]pyrrole (TTF-C4P) donor enforces a host conformation that favors electron transfer to a bisimidazolium quinone (BIQ^{2+}) guest acceptor. In contrast, the addition of a tetraethylammonium cation, which binds more effectively than the BIQ^{2+} guest in the TTF-C4P cavity, leads to back electron transfer, restoring the initial oxidation states of the donor and acceptor pair. The products of these processes were characterized via spectroscopy and x-ray crystallography.

Reversible electron-transfer (ET) processes play a key role in biological energy conversion. Often these events are controlled by external cofactors, including small ions, which favor either charge separation or recombination. For instance, in the O_2-evolving complex of photosystem II, Ca^{2+} and Cl^- are known to be essential activators for the fast turnover of water oxidation, whereas other ionic species can act as activators, inhibitors, or simple spectators (*1*–*5*). Redox-inactive metal ions, such as Ca^{2+}, are known to control the reactivity of organic electron acceptors by binding to the one-electron reduced species involved, that is, radical anions of electron acceptors (*6*). Likewise, the key enzyme in respiration, cytochrome c oxidase, is a heme-copper oxidase with a positively charged protein surface that allows for the binding of a variety of anions with different affinities and stoichiometry (*7*). This recognition process has been reported to induce a redox-dependent structural change that affects the ET process (*8*). However, in spite of the pivotal role of ions as regulators of biological ET (*1*–*8*), anions and cations have rarely, if ever, been exploited to effect reversible ET processes in a simple donor-acceptor (D/A) ensemble.

Here, we report a supramolecular system, based on a tetrathiafulvalene calix[4]pyrrole (TTF-C4P, **1**) donor (*9*) and a dicationic bisimidazolium quinone (BIQ^{2+}, **2**) acceptor (*10*), wherein the judicious addition of anions or cations is used to control the direction of electron transfer. The ability to manipulate the ET process under simple thermal, as opposed to light-induced, conditions has allowed for the isolation and full characterization of both the stable radical products and the putative supramolecular intermediates.

TTF-C4P is an electron-rich calix[4]pyrrole (*9*, *11*–*13*), a class of fluxional tetrapyrrolic macrocycles that are known to bind selected anions well in organic solvents (*11*). As a general rule, anion binding to calix[4]pyrroles induces a change from the so-called 1,3-alternate (Fig. 1 left) to the cone conformation (Fig. 1 center) because of concerted hydrogen bonding interactions. In the particular case of **1**, large electron-deficient species, such as C_{60}, can be bound by the anion-induced bowl-like cone conformation (*12*, *13*). As is true for other calix[4]pyrroles (*14*), within-the-bowl binding of small cations is also seen; this has been established explicitly in the case of tetraethylammonium chloride (TEACl) by proton nuclear magnetic resonance spectroscopy in $CDCl_3$ as well as by x-ray diffraction analysis (figs. S1 and S6).

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Taken in concert, these observations led us to consider that **1**, if combined with a stronger electron acceptor than C_{60}, could create an ET system whose properties may be controlled through the use of various anions and cations. This concept is summarized graphically in Fig. 1. BIQ^{2+} (**2**) was chosen as the redox partner for **1** for several reasons. First, **2** is relatively large; as such, it was expected to be complexed by **1** but only when this latter receptor is in its anion-bound cone conformation. Second, the dicationic nature of **2** suggested to us that, after formation of the proposed donor-acceptor complex **3**, ET would take place to give first the encapsulated product **3′** and then the individual radical species, that is, $[TTF\text{-}C4P]^{\bullet+}$ and $BIQ^{\bullet+}$ (**4** and **5** in Fig. 1). Lastly, in combination with **1**, **2** was expected to act as an electron acceptor and provide a near-isoergonic redox couple as inferred from cyclovoltammetric studies (figs. S26 and S27 and table S3). This, we postulated, would allow us to observe readily the effects of anions, cations, and conformational switching on a potentially reversible thermal electron-transfer process.

Five specific salts of **2** were selected for study; they encompass two subgroups, namely anions that bind well to **1** [$X^- = MeSO_4^-$ (**2a**), Br^- (**2b**), or Cl^- (**2c**); shown in green in Fig. 1] and those that do not [$X^- = BF_4^-$ (**2d**) or PF_6^- (**2e**), shown in red] (fig. S20). As expected, these species reacted very differently with **1**.

For instance, adding increasing amounts of $BIQ^{2+}2X^-$ ($X^- = MeSO_4^-$, Br^-, or Cl^-) salts into a chloroform solution of **1** at the same starting concentration resulted in the gradual emergence of absorption features centered at 751 nm and ~2000 nm at the expense of the original **1** absorption band (λ_{max} = 329 nm) with a clear isosbestic point at 340 nm for $MeSO_4^-$ and Br^- and 338 nm for Cl^- (fig. S17, a to c). Similar spectral changes were observed when tetrahexylammonium chloride (THACl) was added to a mixture of **1** and **2e** (or **2d**) (Fig. 2A) but not when **1** was mixed with **2e** or **2d** in the absence of $MeSO_4^-$, Br^-, or Cl^- (fig. S17, d and e).

On the basis of direct oxidation and spectroelectrochemical experiments, isolation and characterization of the radical salts $[TTF\text{-}C4P]^{\bullet+}MeSO_4^-$ and $[BIQ]^{\bullet+}MeSO_4^-$ (figs. S12 to S19), and literature reports involving simple TTF species (*15*), we ascribed the signals at ~751 and ~2000 nm to $[TTF]_2^{\bullet+}$ radical cation-containing species derived from **1**. New spectral features at ~380 nm were also assigned to the reduced radical $BIQ^{\bullet+}$ in this way (figs. S12b and S14).

No further changes in these optical features were observed under ambient conditions. However,

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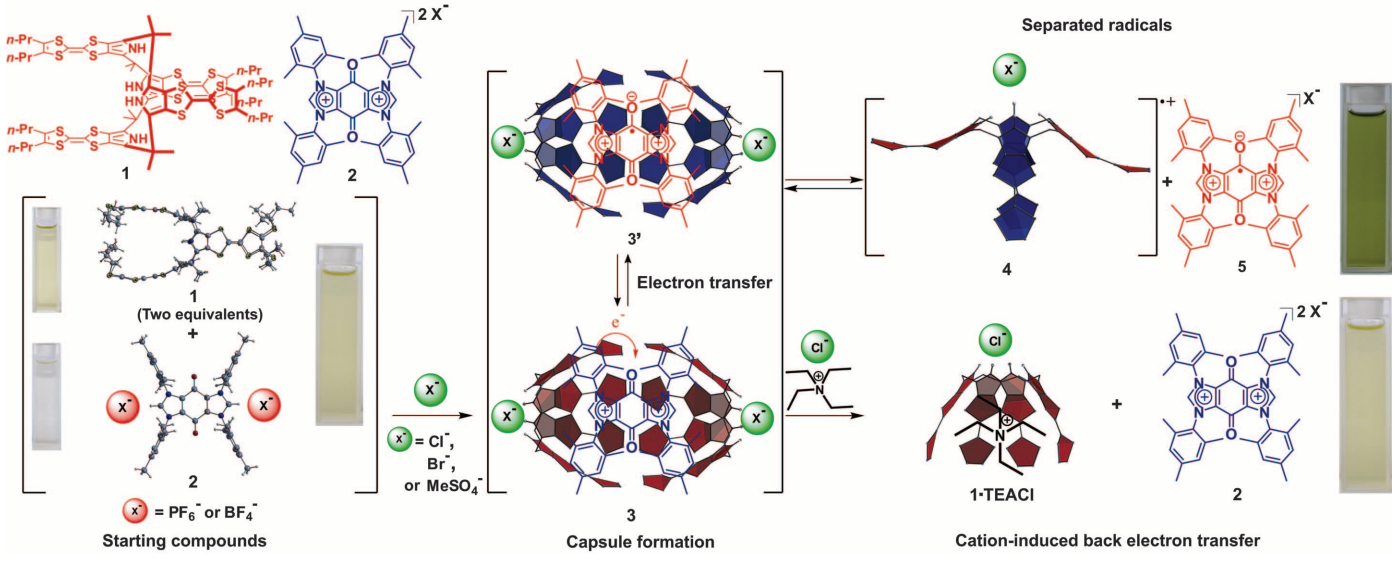

Fig. 1. Chemical structures of **1** and **2** salts and their proposed ion-mediated ET reactions.

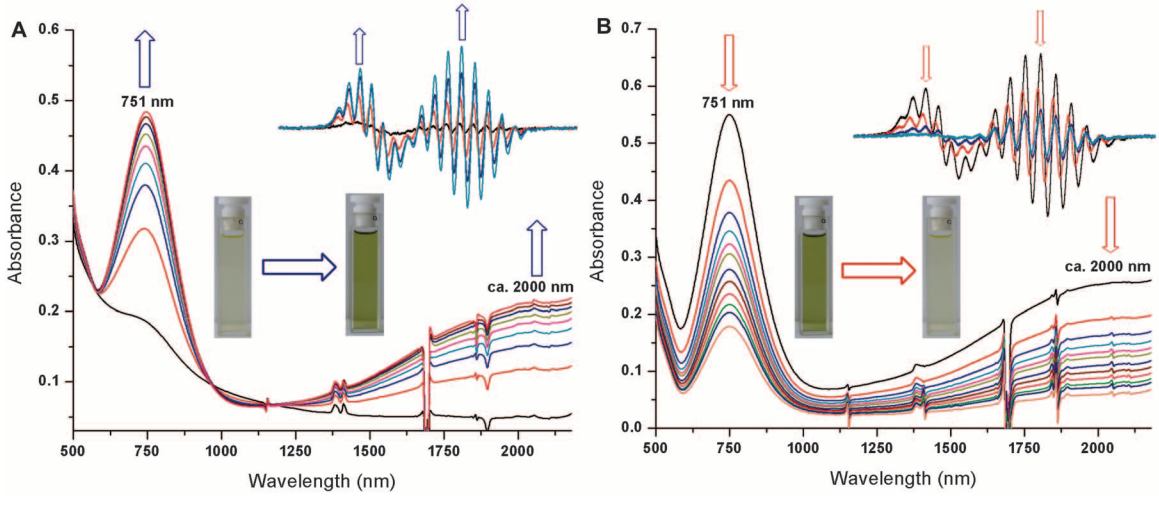

Fig. 2. (**A**) Spectroscopic changes observed when **1** (30 μM in $CHCl_3$) is treated first with 1 molar equiv. of $BIQ^{2+}2PF_6^-$ and then with increasing quantities of THACl in $CHCl_3$ (up to 10 equivalents). (Inset) The EPR spectra of 1:1 mixture of TTF-C4P and $BIQ^{2+}2PF_6^-$ (1.1×10^{-4} M in each) in $CHCl_3$ at room temperature and upon addition of THACl. (**B**) Cation-induced reverse electron transfer seen upon the addition of up to 15 equiv. of TEACl to a 1:1 solution of TTF-C4P and $BIQ^{2+}2Cl^-$ in $CHCl_3$ (30 μM in each). (Inset) EPR spectra of a 1:1 mixture of TTF-C4P and $BIQ^{2+}2Cl^-$ (1.1×10^{-4} M in each) in $CHCl_3$ at room temperature upon addition of up to 5 molar equiv. of TEACl.

the deliberate addition of TEACl, which was expected to bind more effectively than the BIQ^{2+} guest in the TTF-C4P cavity, caused the intensity of the signals at ~751 and ~2000 nm to decrease and the peak at ~329 nm to be restored (Fig. 2B).

Further comparisons, involving a series of ammonium salts containing the tetra(ethyl, butyl, and hexyl)-ammonium cations (TEA^+, TBA^+, and THA^+), were carried out to assess the effect of cation size. It was found that the smaller and more charge-dense cations act as efficient inhibitors for the forward ET process (i.e., $TEA^+ > TBA^+ > THA^+$). As expected, this effect was found to correlate with the ability to bind to the electron-rich TTF-C4P concave pocket; that is, the association constant (K_a) for binding of TEA^+ is larger than the K_a for TBA^+, which is larger than the K_a for THA^+ (figs. S19 and S20). Taken in concert, the observed optical changes are thus fully consistent with the anion-induced formation of an ET state consisting of **5** and **4** and its subsequent cation-triggered reversal. Washing with water can be used to remove the cation salt and regenerate the ET state, **4** and **5** (fig. S30).

Electron paramagnetic resonance (EPR) spectroscopy confirmed that the underlying ET processes involved radical species and facilitated tracking the changes that occurred as first coordinating anions (e.g., Cl^-) and then small cations (i.e., TEA^+) were added (compare the insets to Fig. 2). There are two distinct radical signals in a 1:1 ratio corresponding to the radical cation of **1** at $g = 2.0083$, and the reduced radical of **2** at $g = 2.0056$ (fig. S23). These assignments were confirmed by independent analyses of **4** and **5** obtained through chemical oxidation and electrochemical reduction, respectively. Integration of the EPR spectrum revealed ≥90% conversion to the radical products when **1** was mixed with 2 equivalents (equiv.) of **2a**. In contrast, ≤10% conversion was seen in the case of **1** and 2 equiv. of **2e** (figs. S21 to S23).

The same mixed EPR spectra, containing signals for both **4** and **5**, were obtained when **1** was mixed with **2a**, **2b**, or **2c** in chloroform and when **1** was treated with **2d** or **2e** followed by THACl (Fig. 2A inset). On the other hand, the addition of 2 molar equiv. of TEACl [containing the small TEA^+ cation known (*14*) to bind within the calix[4]pyrrole bowl of **1**] to the 1:1 mixture of **1** and **2c** in chloroform at 298 K caused the EPR signals for **4** and **5** to disappear almost entirely (Fig. 2B inset).

Single crystals were grown through the slow diffusion of hexanes into an equimolar mixture of **1** and **2a** to **2e** in chloroform. In the cases of **2d**, $BIQ^{2+}2BF_4^-$, and **2e**, $BIQ^{2+}2PF_6^-$, only yellow crystalline solids corresponding to the starting materials were isolated (*16*). In contrast, from the reactions of **1** with **2a** to **2c**, three sets of crystals were individually separated according to the method of Pasteur and independently characterized via x-ray diffraction analysis (fig. S4). One set of crystals corresponded to $[TTF\text{-}C4P]^{\bullet+}MeSO_4^-$ (**4a**, Fig. 3A) and a second to $[BIQ]^{\bullet+}MeSO_4^-$ (**5a**, Fig. 3B). We assigned these structures to products of the electron-transfer reaction on the basis of the number of counter ions and prominent structural parameters, such as elongated C–O distances in **5a** and **5b** (1.25 Å versus 1.15 Å in **2a**) (*16*) and the short interplanar distance of 3.4 Å seen in the case of $[TTF\text{-}C4P]^{\bullet+}MeSO_4^-$ (**4a**). Similar products have been proposed in solution (*15*).

Structural analysis of the third set of crystals revealed a supramolecular D/A assembly, wherein two anion-bound bowl-like TTF-C4P moieties tightly encapsulate a BIQ guest (Fig. 4A). On the basis of the structural parameters, these capsule species are considered to be tightly coupled $[TTF\text{-}C4P]_2^{\bullet+}/[BIQ]^{\bullet+}2X^-$ biradical systems (**3′b** and **3′c**) (table S2).

The existence of a tightly coupled biradical capsule was further confirmed by low-temperature (4-K) EPR analyses of a single crystal of the $[TTF\text{-}C4P]_2^{\bullet+}/[BIQ]^{\bullet+}2Cl^-$ salt (**3′c**, Fig. 4B). Typical triplet signals were observed at $g = 4.08$ and 2.007 with zero-field splitting. When plotted against the angle of rotation for the single crystal, the observed zero-field splitting parameter (D) resulted in a sinusoidal curve; this is fully consistent with the existence of an intramolecular radical ion pair.

On the basis of the above findings, we propose that anion-induced electron transfer takes place in accord with Fig. 1. Specifically, addition of a **2** salt containing a coordinating anion (or else THACl in tandem with **2** salts of noncoordinating anions) to a solution of **1** in chloroform leads first to conformational flipping and stabilization of the calix[4]pyrrole cone conformation. This is followed by formation of a capsulelike D/A complex, **3**, followed by fast ET. The initial, within-the-capsule ET (to give **3′**) is then followed by separation of the two positively charged radical species in question (**4** and **5**). The net result is the formation of **4** and **5** as ET products through an equilibrium process.

An initial kinetic study of the ET process provides support for this conclusion. For instance, as would be expected for a within-capsule ET process, the observed rate constants exhibit saturation behavior as the concentration of **1** increases.

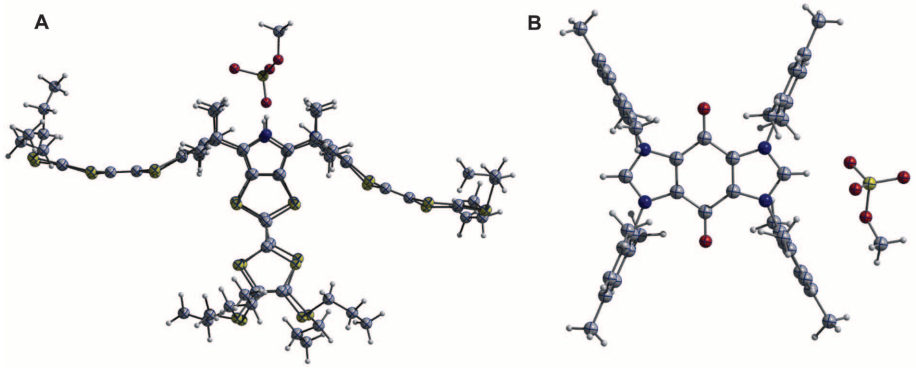

Fig. 3. Single-crystal x-ray structures of the radical products obtained from the mixture of **1** and $BIQ^{2+}2MeSO_4^-$ (**2a**). (**A**) $[TTF\text{-}C4P]^{\bullet+}MeSO_4^-$ (**4a**); (**B**) $[BIQ]^{\bullet+}MeSO_4^-$ (**5a**).

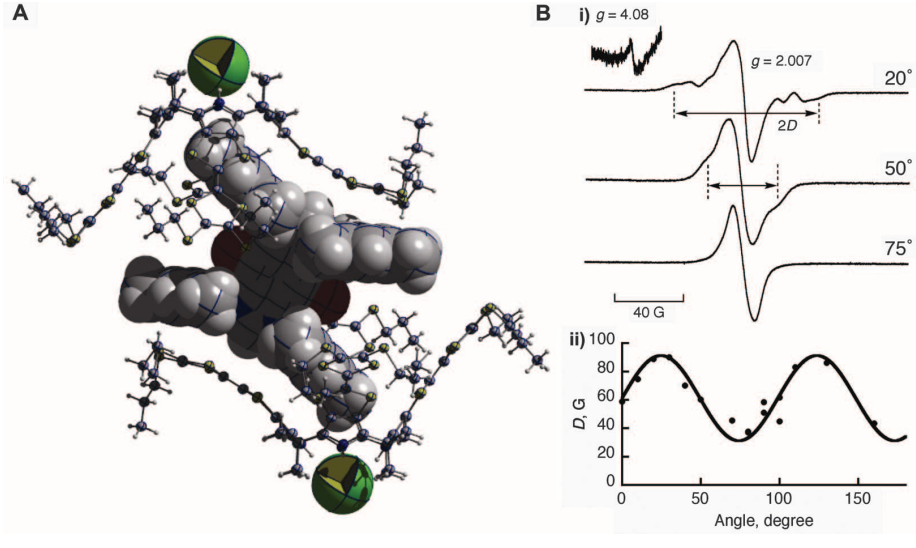

Fig. 4. (**A**) Single-crystal x-ray structure of the supramolecular radical ion pair complex of net stoichiometry $[TTF\text{-}C4P]_2^{\bullet+}/[BIQ]^{\bullet+}2Cl^-$ (**3′c**). (**B**) (i) EPR spectra of a crystal identical to that used in **3′c** recorded at different rotation angles at 4 K by using a goniometer. (ii) Plot of D versus rotation angle for the EPR spectrum of the single crystal; D values calibrated by using Mn^{2+} markers.

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The rate constant associated with the production of **4** was determined and found to be 9.3 s^{-1} at 233 K (figs. S24 and S25).

We ascribe the ET process induced by a coordinating anion to both the increased driving force that results from anion binding and a conformational change that accelerates the reaction via formation of a supramolecular assembly involving the anion-bound form of **1** and **2** (proposed intermediate **3**) that then produces **4** and **5** via the intermediate product **3′**. Likewise, we rationalize the reversal of the ET process to destabilization of the resulting radical species (relative to the neutral cation-bound form, **1•TEACl**) in the presence of a competing cation. Support for the driving force considerations comes from the negative and positive shifts (by ~60 and 120 mV, respectively) seen in the one-electron oxidation peak when 2 equiv. of $THAMeSO_4$ (where Me is a methyl group) and 10 equiv. TEACl were added to solutions of **1** [oxidation potential (E_{ox}) = 310 mV versus a Ag/AgCl reference electrode; 0.1 M $THAPF_6$] and **1** + 2 equiv. of THACl, respectively (figs. S28 and S29 and tables S4 and S5). In contrast, the value of the one-electron reduction potential (E_{red}) of **2** (325 mV versus a Ag/AgCl reference electrode; 0.1 M $THAPF_6$) proved insensitive to the conditions (fig. S27).

We have detailed a supramolecular ET process that is controlled by a mechanism frequently exploited by nature, namely external ion modulation. The ionic cofactors in our artificial ion-mediated ET system not only induce substantial structural changes, but also control the exergonicity of the ET reaction. Similar structural control of the energetics of ET reactions may constitute one role of ionic cofactors in natural systems.

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16. Materials and methods are detailed in supporting material on *Science* Online. Details of cyclic voltammetric, near-infrared–visible spectral, and x-ray crystallographic studies (**1**, **2a**, **2b**, **2e**, **4a**, **5a**, **5b**, **3′b**, **3′c**, and **1•TEACl**) are included.

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Supporting Online Material

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Materials and Methods
Figs. S1 to S30
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Nonthermal Current-Stimulated Desorption of Gases from Carbon Nanotubes

Amin Salehi-Khojin, Kevin Y. Lin, Christopher R. Field, Richard I. Masel*

The desorption of gases from carbon nanotubes is usually a slow process that limits the nanotubes' utility as sensors or as memristors. Here, we demonstrate that flow in the nanotube above the Poole-Frenkel conduction threshold can stimulate adsorbates to desorb without heating the sensor substantially. The method is general: alcohols, aromatics, amines, and phosphonates were all found to desorb. We postulate that the process is analogous to electron-stimulated desorption, but with an internally conducted rather than externally applied source of electrons.

Single-walled carbon nanotubes (SWNTs) have been proposed for a wide range of applications (*1*–*5*), including as sensors for a variety of gases, or as a component in nanotube-based electronics. In general, SWNT-based sensors have the key advantages of low power, high sensitivity, and very small size (*5*).

Figure 1 shows a diagram of our nanotube sensors. They consist of a nanotube network between two gold contacts. They are of a standard design, except that we use defected nanotubes to enhance sensitivity (*6*). Our fabrication procedure also gives unusually small contact impedances (*6*, *7*).

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One of the challenges in SWNT-based sensor design is the slow recovery of the nanotube resistance after gases adsorb. Figure 2 shows the response of a typical bare nanotube sensor to a 100-ms pulse containing 10^{17} molecules of toluene in helium at 24°C. The sensor shows an immediate step change in voltage. There is also an initial peak superimposed on the step. The step does not recover, even after a nearly 1-hour waiting period.

Physically, toluene exhibits multiple binding modes at different sites on the carbon nanotubes (*8*). Some of the molecules are irreversibly adsorbed at room temperature, whereas others are only weakly bound. We attribute the step change in voltage to the toluene that irreversibly adsorbs on the SWNTs. Such a step change could also, in principle, occur because of changes to contact impedance at the gold-nanotube contacts, but in our sensors the impedance is less than 0.002 V (*6*) and does not change measurably when gas adsorbs or when a 12-V potential is applied to the sensor. This step behavior is a hindrance to reuse of SWNT sensors. There are reports of accelerated recovery for a given class of molecules upon coating the sensor with polymers (*9*), but then other molecules irreversibly adsorb, and decrease sensitivity.

Here, we demonstrate the removal of gases from nanotubes via a distinct process that we have termed current-stimulated desorption (CSD). In CSD, a current applied through the sensor stimulates molecular desorption. Electron-stimulated desorption is a well-known related process, but has only been demonstrated with an external source of electrons or photons (*10*–*15*).

This discovery arose through our study of the influence of electron transport mode on the performance of nanotube sensors (*6*). Three main mechanisms of electron transport in nanotubes have been established: quantum tunneling (*16*–*18*), Schottky-Richardson conduction (*19*–*22*), and Poole-Frenkel conduction (*23*–*27*). At low electric fields, quantum tunneling dominates. Electrons travel by tunneling between quantum states in the nanotube. Currents are small, but resistances are, too. Increasing the electric field leads to Schottky-Richardson conduction (*19*–*22*), in which transport occurs mainly within the conduction band of the nanotube. At higher voltages and currents, a third transport mechanism, called Poole-Frenkel conduction, begins to dominate (*23*–*27*). In this regime, electrons jump over defects in the surface of the nanotubes due to

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high local electric fields and then continue along the nanotube. Electrons can also skip between molecules adsorbed onto a nanotube.

Our objective was to see if Poole-Frenkel conduction could be used to stimulate molecules to desorb. Madey and Yates (*10*, *13*) demonstrated that desorption can be induced by electronic excitations of an adsorbate, at energies of 2 to 5 eV. There are also reports of photodesorption of molecules from carbon nanotubes (*28*–*33*). Generally a 2- or 3-eV photon is sufficient to desorb molecules from surfaces, although in one case, a 1.2-eV photon was sufficient (*33*). One can also get desorption by exciting the molecule vibrationally so that it enters a repulsive state. Poole-Frenkel conduction operates in a comparable energy regime, so it seemed a plausible alternative.

To test this hypothesis, we applied varied current and then measured desorption, via recovery of the nanotube sensor after exposure to a pulse of gas (*6*). We chose this method because the adsorbate layers are too unstable to be probed by electron spectroscopy, and adsorbate coverages were too low for optical probes.

In Fig. 3A, the current-induced voltage was too low to stimulate substantial Poole-Frenkel conduction (*6*). In Fig. 3B, there is some Poole-Frenkel conduction, but insufficient voltage to excite electronic transitions. Figure 3C is an intermediate case, where voltages (3.77 V) are just above the threshold for electronic transitions, and in Fig. 3D there is substantial Poole-Frenkel conduction and the voltages (>12 V) are high enough to desorb many molecules. The sensor shows an irreversible response in Fig. 3, A and B, some recovery in Fig. 3C, and complete recovery in Fig. 3D. Finally, Fig. 3E demonstrates that CSD can be effectively applied 3 hours after the initial exposure and return the sensor rapidly to baseline.

We have reproduced these results with more than 10 different sensors. All show the same slow recovery at low currents and fast response at high currents. We have also observed the effect with a number of other gases. We have demonstrated the effect with methanol, ethanol, 1-propanol, 1-butanol, isopentanol, 1-hexanol, 1-heptanol, dimethyl methylphosphonate, tributylphosphate (TBP), and 1,2-dichlorobenzene (fig. S4). The TBP results were notable because TBP has a vapor pressure of less than 0.1 mm Hg; thus, CSD can remove involatile molecules from the nanotubes.

One has to carefully consider how heating of the nanotubes may have affected the results in Fig. 3. The experiments reported here were designed to minimize heating during the experiment. First, our sample preparation procedure was previously shown to minimize contact resistance, thereby minimizing heating at the contacts (*6*). Sensors were also fabricated on a silicon wafer with a monolayer of 3-aminopropyltriethoxysilane (APTES) applied to improve the thermal contact between the nanotubes and the silicon. Silicon's high thermal conductivity served to further minimize heating of the nanotubes. Calculations indicate that the temperature of the nanotubes should not have risen substantially under these conditions (*34*–*36*).

We also conducted two different experiments to measure the temperature change. First, an infrared imager was used to detect any local temperature rise in the nanotube sensor as current was applied. Figure S1 shows the results. The infrared measurements indicated a less than 4°C temperature rise at the highest currents explored here, and negligible rises at lower currents. Second, Raman spectroscopy was used to confirm the lack of a temperature rise. Zhou *et al*. (*37*) showed that the intensity of the G and D bands of the nanotube spectrum are sensitive to temperature; we did not observe any intensity changes or wavelength shifts of the G and D bands as the current was raised (fig. S2). The spectroscopic measurements put an upper bound on the average temperature change of 13°C.

Next we performed experiments to see if a 13°C change in the nanotubes could cause an observable change in sensor recovery rate. Figure 4 shows how the sensor response varied as the temperature was raised from 24° to 115°C. Increasing the temperature up to 80°C raises the baseline, because the resistance of the sensor increases with temperature (changes in resistance

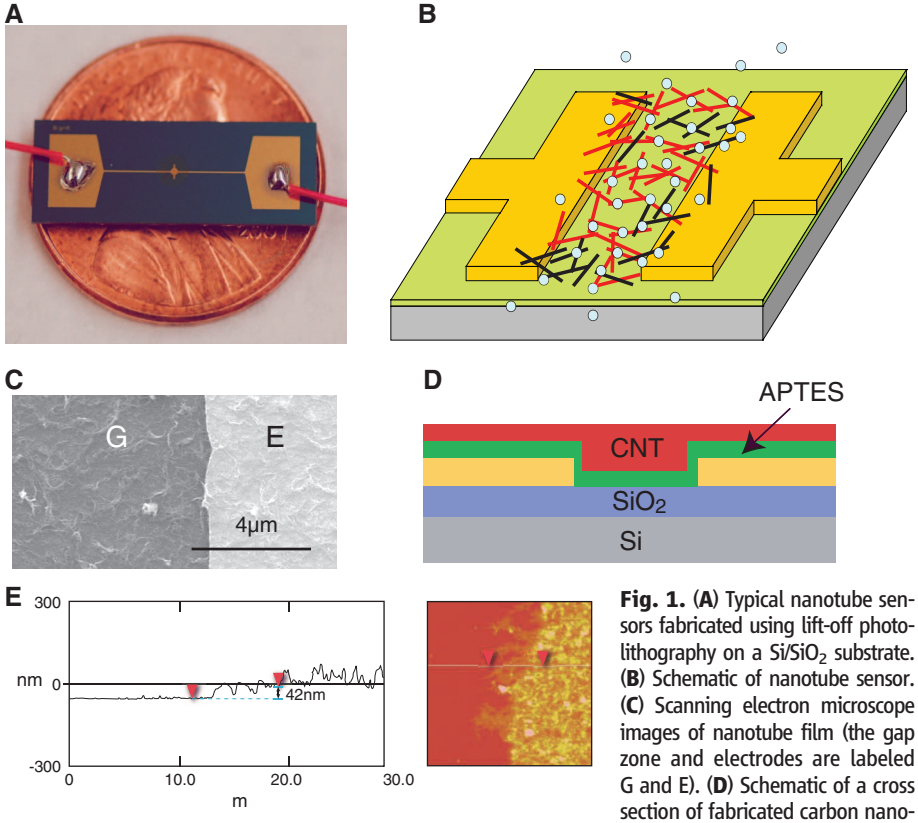
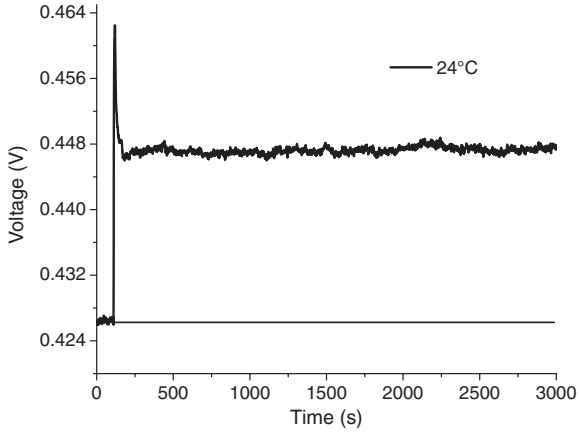


Fig. 1. (**A**) Typical nanotube sensors fabricated using lift-off photolithography on a Si/SiO_2 substrate. (**B**) Schematic of nanotube sensor. (**C**) Scanning electron microscope images of nanotube film (the gap zone and electrodes are labeled G and E). (**D**) Schematic of a cross section of fabricated carbon nanotube (CNT) sensors. (**E**) Typical atomic force microscopy characterization showing an average nanotube thickness of ~42 nm.

Fig. 2. Typical response of a nanotube sensor to toluene molecules, measured by applying 50 μA to the sensors and measuring the voltage drop across them as a function of time. The response consists of two components: a sharp peak and a step change.



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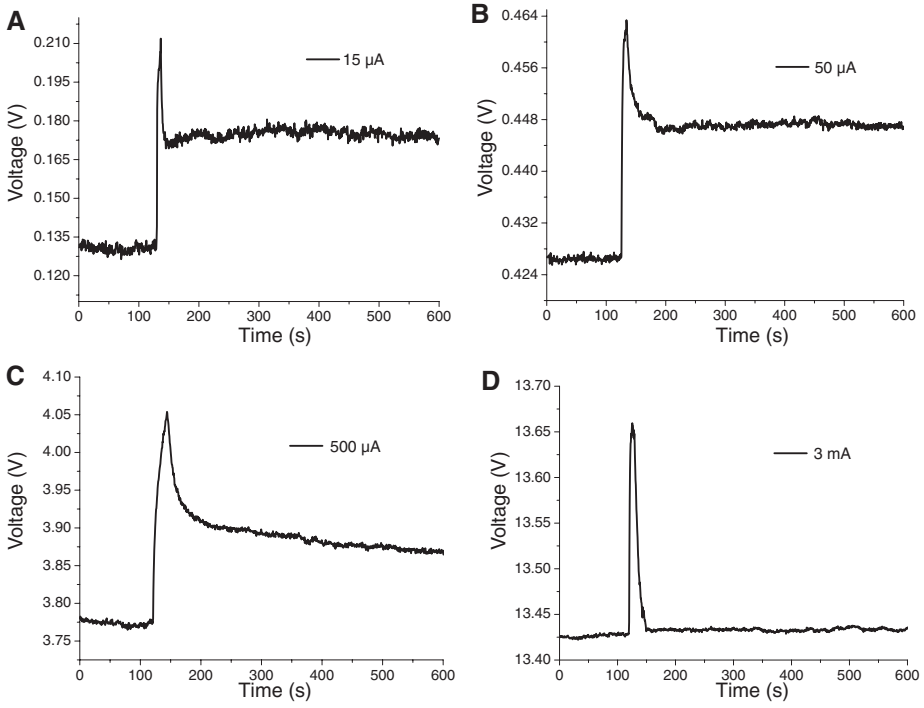

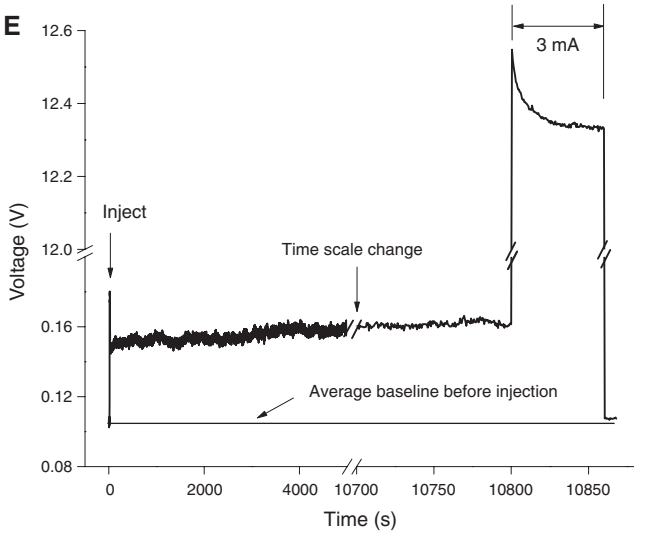

Fig. 3. (**A** to **D**). Response of the nanotube sensor to toluene molecules at four different applied currents (15 μA, 50 μA, 500 μA, and 3 mA) at 24°C. At low currents, there are two components to the recovery: a rapid decay over tens of seconds and a slower one over hours to days. As the current through the nanotube rises to the Poole-Frenkel conduction threshold, the full recovery speeds up to a ~1-min time scale. (**E**) A test in which toluene is injected and a 15-μA current maintained for 10,800 s (3 hours), after which the current is raised to 3 mA for 60 s and then lowered to 15 μA. The horizontal line in the figure is the average baseline before the process starts. As shown, current almost completely recovers. Also shown is the horizontal scale change in (E) before 10,700 s.

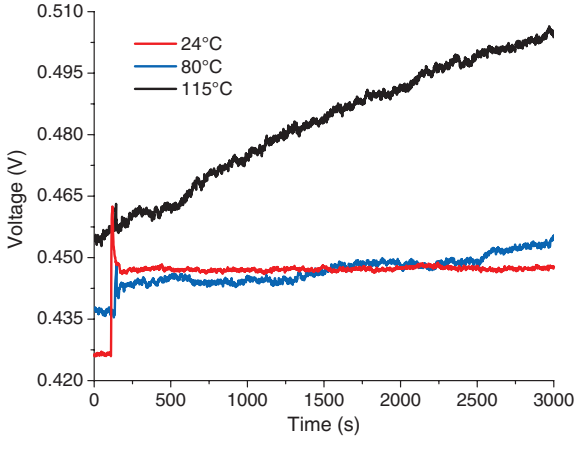

Fig. 4. Typical response of a nanotube sensor to toluene molecules, measured by applying 50 μA to the sensors and measuring the voltage drop across them as a function of time. Even at 80°C, the voltage does not return to baseline after 3500 s. The response does recover at 115°C, but the sensor quickly degrades at that temperature, resulting in the observed slope. An expanded view of the data is shown in fig. S3.

cause voltage changes in constant current measurements), but there is still an irreversible component of the response. In addition, the sensor shows slow degradation, as indicated by the slope of the plot. The irreversible component of the response disappears when the sensor degrades severely, as manifested by the continuously rising baseline. The stability of the baseline in Fig. 3 shows that simply applying a current of 3 mA does not induce such thermal behavior. We could not reproduce the CSD response by heating the sensor to any temperature.

Furthermore, local temperature changes greater than 80°C can be ruled out. Kumar *et al*. have shown with thorough calculations (*36*) that the thermal conductivity of SWNTs is sufficiently high to quickly dissipate a 50°C temperature gradient across the length of our sensors. Thus, if there were a hot spot created in the sensor, an extensive portion of the sensor would heat up, a result not supported by the infrared imaging and spectroscopic data.

Finally, desorption is not a local phenomenon in our data. If molecules were being thermally desorbed only from small regions of the nanotube network, then only those areas would manifest fast recovery, while the rest of the sensor recovered slowly. We observe fast recovery over the entire sensor, implying that desorption is occurring over the entire surface of the network and could not be associated with local hot spots.

Consequently, we conclude that the accelerated recovery time observed in Fig. 3 is not due to heating of the nanotubes. Instead, it must be due to a nonthermal process whereby the analyte is removed from the nanotube surface in response to the current.

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38. This work was supported by grants from Cbana Laboratories and Dioxide Materials. C.R.F. developed the sensor fabrication method that allowed the measurements to be made. K.Y.L. took most of the data. A.S.-K. directed much of the data acquisition and worked with R.I.M. to understand how Poole-Frenkel conduction would affect nanotube sensor response. R.I.M. wondered if current stimulated could occur and asked A.S.-K. to devise experiments to see if it did occur. R.I.M. and A.S.-K. drafted the paper. The authors are submitting patents based on some aspects of the work.

Supporting Online Material

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Materials and Methods
Figs. S1 to S4
References

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Future CO_2 Emissions and Climate Change from Existing Energy Infrastructure

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Slowing climate change requires overcoming inertia in political, technological, and geophysical systems. Of these, only geophysical warming commitment has been quantified. We estimated the commitment to future emissions and warming represented by existing carbon dioxide–emitting devices. We calculated cumulative future emissions of 496 (282 to 701 in lower- and upper-bounding scenarios) gigatonnes of CO_2 from combustion of fossil fuels by existing infrastructure between 2010 and 2060, forcing mean warming of 1.3°C (1.1° to 1.4°C) above the pre-industrial era and atmospheric concentrations of CO_2 less than 430 parts per million. Because these conditions would likely avoid many key impacts of climate change, we conclude that sources of the most threatening emissions have yet to be built. However, CO_2-emitting infrastructure will expand unless extraordinary efforts are undertaken to develop alternatives.

If current greenhouse gas (GHG) concentrations remain constant, the world would be committed to several centuries of increasing global mean temperatures and sea level rise (*1*–*3*). By contrast, near-elimination of anthropogenic CO_2 emissions would be required to produce diminishing GHG concentrations consistent with stabilization of mean temperatures (*4*–*6*). Yet long-lived energy and transportation infrastructure now operating can be expected to contribute substantial CO_2 emissions over the next 50 years [e.g., (*7*)]. Barring widespread retrofitting of existing power plants with carbon capture and storage (CCS) technologies or the early decommissioning of serviceable infrastructure, these "committed emissions" represent infrastructural inertia, which may be the primary contributor to total future warming commitment.

Emissions scenarios such as those produced by the Intergovernmental Panel on Climate Change (IPCC) rely on projected changes in population, economic growth, energy demand, and the carbon intensity of energy over time (*8*). Although these scenarios represent plausible future emissions trends, the infrastructural inertia of emissions at any point in time is not explicitly quantified. Here, we present scenarios reflecting direct emissions from existing energy and transportation infrastructure, along with climate model results showing the warming commitment of these emissions.

With respect to GHG emissions, infrastructural inertia may be thought of as having two important and overlapping components: (i) infrastructure that directly releases GHGs to the atmosphere, and (ii) infrastructure that contributes to the continued production of devices that emit GHGs to the atmosphere. For example, the interstate highway and refueling infrastructure in the United States facilitates continued production of gasoline-powered automobiles. Here, we focus only on the warming commitment from infrastructure that directly releases CO_2 to the atmosphere. Essentially, we answer the following question: What if no additional CO_2-emitting devices (e.g., power plants, motor vehicles) were built, but all the existing CO_2-emitting devices were allowed to live out their normal lifetimes? What CO_2 levels and global mean temperatures would we attain? Of course, the actual lifetime of devices may be strongly influenced by economic and policy constraints. For instance, a ban on new CO_2-emitting devices would create tremendous incentive to prolong the lifetime of existing devices. Thus, our scenarios are not realistic, but they offer a means of gauging the threat of climate change from existing devices relative to those devices that have yet to be built.

The details of our analytic approach are described in (*9*). In summary, we developed scenarios of global CO_2 emissions from the energy sector (*10*) using data sets of power plants (*11*, *12*) and motor vehicles (*13*) worldwide, as well as estimates of fossil fuel emissions produced directly by industry, households, businesses, and other forms of transport (*14*). We estimated lifetimes and annual emissions of infrastructure from historical data. Non-energy emissions (e.g., from industrial processes, land use change, agriculture, and waste) were taken from the IPCC's Special Report on Emissions Scenarios (*8*). We projected changes in CO_2 and temperature in response to our calculated emissions with the use of an intermediate-complexity coupled climate-carbon model, the University of Victoria Earth System Climate Model (*9*).

Cumulatively, we estimate that 496 (282 to 701 in lower- and upper-bounding scenarios) gigatonnes of CO_2 (Gt CO_2; 1 Gt = 10^{12} kg) (*9*) will be emitted from the combustion of fossil fuels by existing infrastructure between 2010 and 2060 (Fig. 1, A and B). Adding emissions from non-energy sources, climate model results indicate that these emissions would allow the atmospheric concentration of CO_2 to stabilize below 430 parts per million (ppm), with mean warming of 1.3°C (1.1° to 1.4°C) above the pre-industrial era (or 0.3° to 0.7°C greater than at present; Fig. 1, C and D). Excluding emissions from non-energy sources, atmospheric CO_2 emissions would

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stabilize below 415 ppm, with mean temperatures 1.2°C (1.1° to 1.3°C) greater than the pre-industrial era. By comparison, scenarios that assume continued expansion of fossil fuel–based infrastructure predict cumulative emissions of 2986 to 7402 Gt CO_2 during the remainder of this century (*8*), leading to warming of 2.4° to 4.6°C by 2100 and atmospheric concentrations of CO_2 greater than 600 ppm (*15*).

We note that 450 ppm and 2°C are climate stabilization benchmarks with substantial currency in international negotiations (*16*, *17*). It is important to recognize that direct emissions from existing infrastructure will not cause these levels to be exceeded. Insofar as the key vulnerabilities of geophysical, biological, and socioeconomic systems manifest themselves beyond these benchmarks (*18*), the primary threats posed by climate change are a consequence of emissions from devices that do not yet exist.

Of the 1326.7 GW of generating capacity built worldwide since 2000, 416.3 GW (31.4%) are generated from coal, 449.1 GW (33.9%) from natural gas, and 47.5 GW (3.6%) from oil (*11*) (fig. S1A). Construction of nuclear power plants, the largest source of carbon-free energy, has declined markedly since peaking in the 1980s, constituting only 29.5 GW (2.2%) of generating capacity installed worldwide since 2000 (*11*). During the same period, other carbon-free energy sources (wind, solar, hydroelectric, geothermal) together account for 231.0 GW (17.4%) of commissioned generating capacity (*11*).

Historical data from 4573 retired generators indicate that the mean lifetimes of facilities burning coal, natural gas, and oil are 38.6, 35.8, and 33.8 years, respectively [compare with (*19*)]. It is the combination of these long lifetimes and a predominant share of annual emissions (46.3% in 2007) (*14*) that results in the largest commitment to future emissions: a cumulative 224 (127 to 336) Gt CO_2 from primary energy infrastructure before 2060 (Fig. 1A and table S1).

The transport sector represents the next largest share of annual CO_2 emissions (22.9% in 2007) (*14*). Globalization and rapid economic growth in China and other emerging markets have greatly expanded the global transport sector in the past decade. Moreover, transport infrastructure is fueled almost exclusively by oil, and operating lifetimes can in some cases exceed 30 years. We estimate cumulative committed emissions from transport infrastructure in operation worldwide to be 115 (63 to 132) Gt CO_2.

Of the total transport-related emissions, nearly two-thirds is from road transport (74 Gt CO_2; Fig. 1A). Although motor vehicle sales in Europe and North America have been steady or slightly declining since 2000, surging vehicle sales in China during the same period reflect growth of private vehicle ownership at a rate of ~20% per year (*20*). Between 1990 and 2007, the number of motor vehicles in operation worldwide increased by 56% (*13*), and we estimate the mean age of the global motor vehicle fleet to be 9.7 years (weighted by annual emissions; fig. S1B). Survival rates of late-model vehicles in the United States indicate an average lifetime of 17, 16, and 28 years for passenger cars, light trucks, and heavy vehicles (trucks and buses), respectively. Led by developing economies, emissions from road transport worldwide are projected to continue to grow rapidly over the next several decades (*21*).

Industrial, residential, and commercial infrastructure that burns fossil fuels also represents a considerable commitment to future emissions.

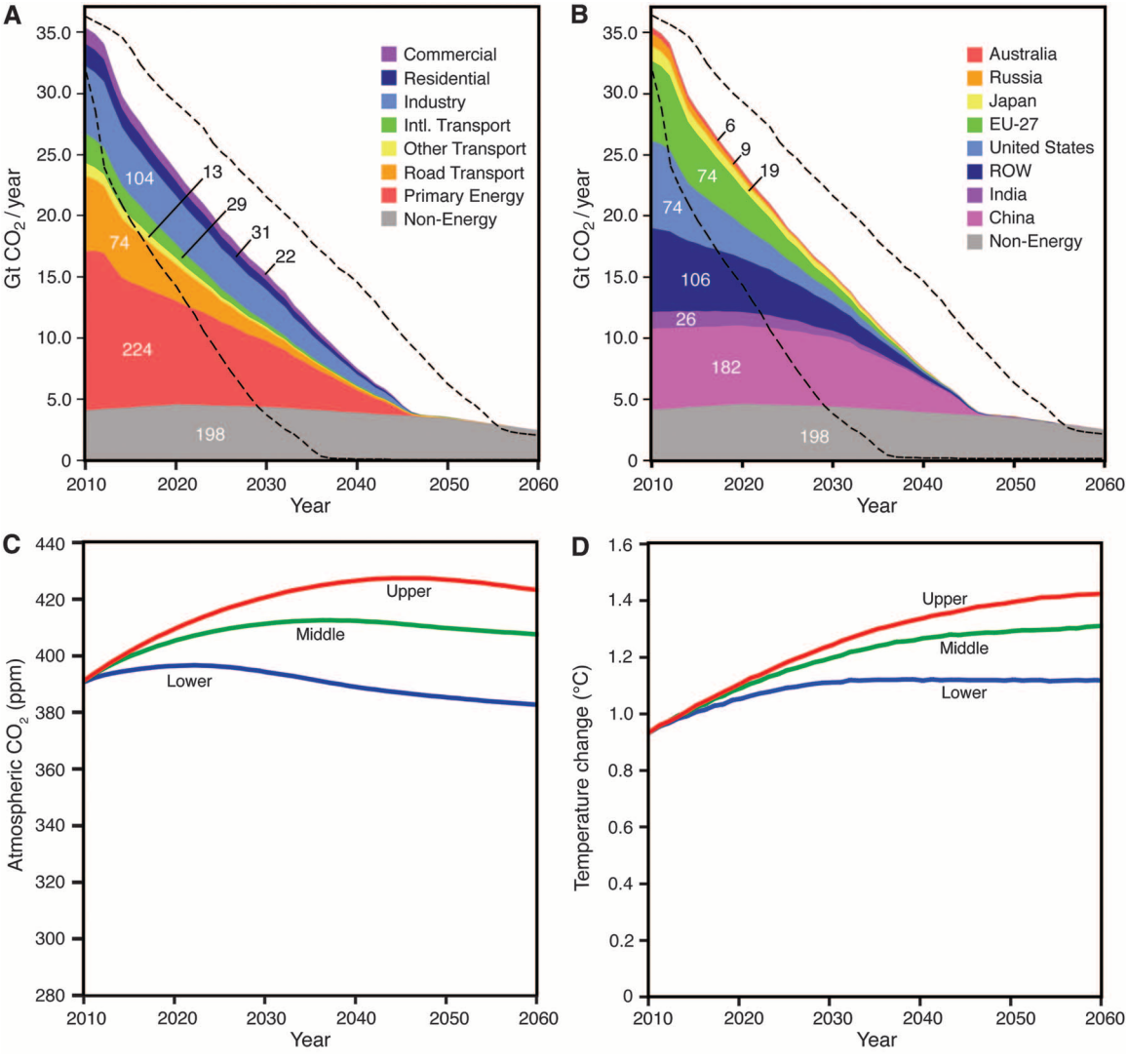

Fig. 1. (**A** to **D**) Scenario of CO_2 emissions from existing energy and transportation infrastructure by industry sector (A) and country/region (B), as well as response of atmospheric CO_2 (C) and global mean temperature (D). In (A) and (B), the non-energy emissions shown are global emissions projected under the IPCC Special Report on Emission Scenarios A2 marker scenario, and dashed lines indicate total emissions from upper- and lower-bounding scenarios. Vertical axis for all panels indicates change from pre-industrial values.

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We estimate the cumulative commitment from industrial equipment to be 104 (61 to 153) Gt CO_2, with residential and commercial infrastructure representing additional emissions of 31 (18 to 47) and 22 (13 to 33) Gt CO_2, respectively (Fig. 1A). Because CO_2-emitting devices in these sectors are generally smaller, more varied, and more numerous than primary energy infrastructure, monitoring of emissions is generally indirect and tied to fuel use. As a result, few data exist on the vintage of existing stocks or expected lifetimes of industrial, residential, and commercial infrastructure. We assume that the vintage and lifetimes are similar to those of primary energy infrastructure, which may overestimate their emissions.

Non-energy emissions, or those unrelated to the combustion of fossil fuels, occur as the result of industrial processes such as the manufacture of cement and steel, where the chemical transformation of feedstocks releases CO_2. Agriculture, waste management, and changing land use also contribute non-energy emissions, as carbon stocks in soils and biomass are oxidized and non-

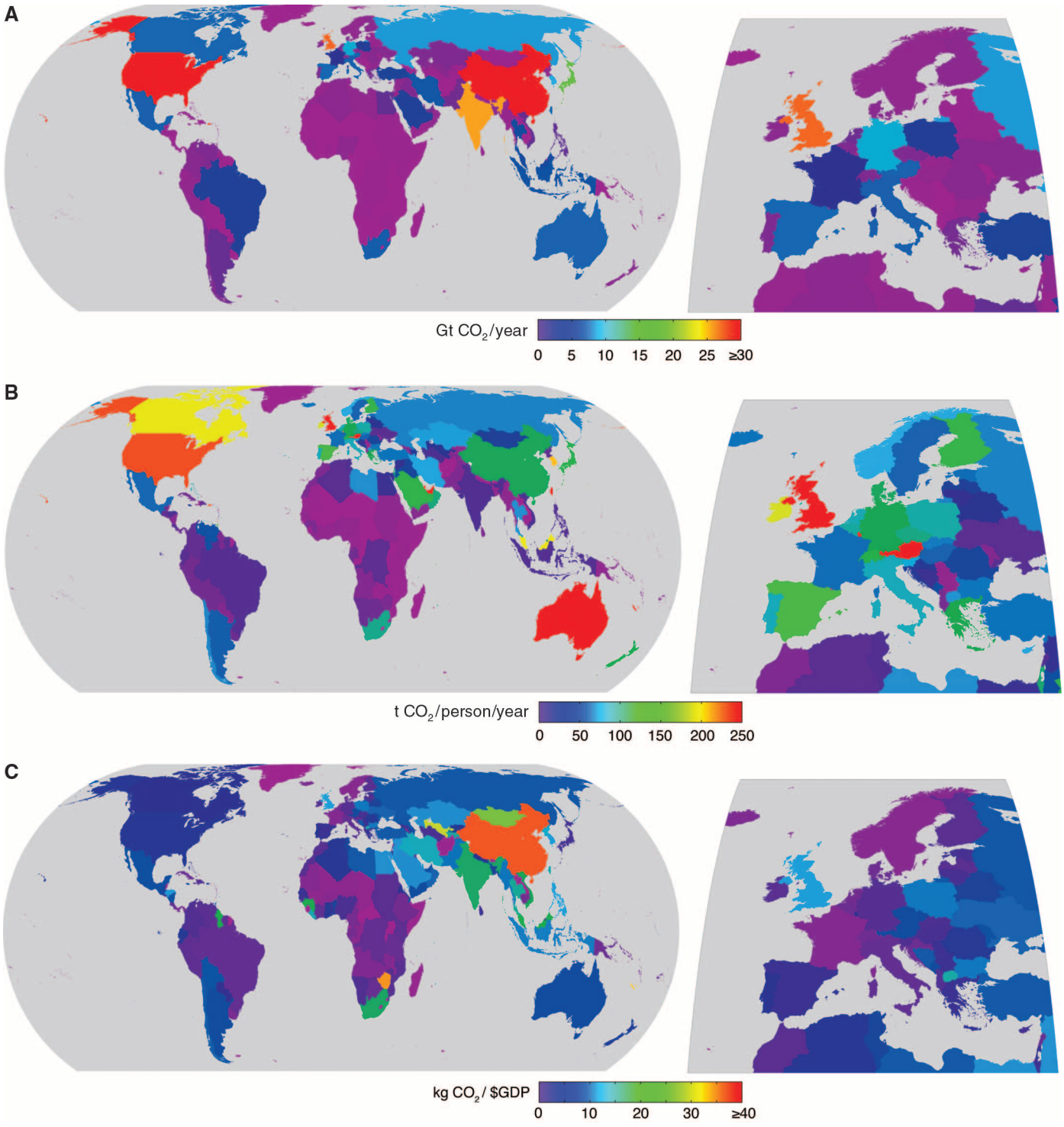

Fig. 2. (**A** to **C**) Regional emissions commitment from existing energy and transportation infrastructure (A), normalized by regional population (B), and normalized by regional GDP (C).

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CO_2 greenhouse gases such as N_2O and CH_4 are produced. Although some of these emissions are dictated by infrastructure, this study focuses only on emissions from the energy sector (including transportation). However, it is plausible that under some combination of CCS technologies, reduced conversion of unmanaged land, and changed agricultural and industrial practices, non-energy emissions could diminish in the future. In view of this possibility and to isolate the contributions of existing energy infrastructure and non-energy emissions, we performed simulations including non-energy emissions from a range of scenarios (*9*) and others in which non-energy emissions were set instantaneously to zero. Excluding non-energy emissions, mean temperatures reach 1.2°C (1.1° to 1.3°C) greater than the pre-industrial era and atmospheric concentrations of CO_2 peak at less than 415 ppm (fig. S2).

Geographically, committed emissions are concentrated in highly developed countries (e.g., western Europe, the United States, Japan) and populous emerging markets in the developing world, particularly China (Figs. 1B and 2A). Infrastructural inertia is greatest in China, where rapid economic development and industrialization in the past decade have led to a prodigious expansion of energy infrastructure. Nearly one-quarter of electrical generating capacity commissioned worldwide since 2000 is in coal-burning plants in China (322.3 GW), and the mean age of power plants operating in China is 12 years (weighted by annual emissions) (*11*, *12*). For these reasons, China alone accounts for roughly 37% of the global emissions commitment: 182 (118 to 244) Gt CO_2 (table S1). Scenarios that allow continued expansion of fossil fuel infrastructure commonly project cumulative emissions from China's primary energy sector to exceed 300 Gt CO_2 this century [e.g., (*20*, *22*)].

In comparison, the mean age of power plants in the United States is 32 years, and generating capacity added since 2000 is predominantly gas-fired (187.6 GW) and wind-generated (28.3 GW), with coal a distant third (8.0 GW). The mean age of Japanese and European power plants is similarly advanced: 21 and 27 years, respectively (*23*). Thus, although current CO_2 emissions from China and the United States are similar in magnitude, the infrastructural commitment to future CO_2 emissions is much greater in China, because China's energy infrastructure is younger than that of the United States, and thus has a longer remaining lifetime. Nonetheless, infrastructure in the United States, Europe, and Japan represents cumulative commitments of 74, 74, and 19 Gt CO_2, representing 15%, 15%, and 4% of the global emissions commitment, respectively (Fig. 1B).

Emissions commitments per capita and per unit GDP are important indicators of global equity that further highlight the uneven distribution of energy services between developed and developing regions (Fig. 2, B and C, and table S2). Despite its much larger population, emissions commitment per capita in China (136 t CO_2 per person) is remarkably similar to that in Japan and Europe (152 and 150 t CO_2 per person, respectively), but still considerably less than the commitment of 241 t CO_2 per person in the United States (Fig. 2B). The comparability of per capita commitments in China and the most developed countries underscores the global importance of future emissions and climate policy in China, but ignores the legacy of historical emissions as well as the role of consumption in developed countries in driving Chinese emissions (*24*). Elsewhere, greater inequities persist: The per capita commitment in India of only 23 t CO_2 per person means that each individual in China and the United States is committed to the same emissions as ~6 and ~10 individuals in India, respectively.

In contrast, committed emissions per unit GDP in both China and India (38.3 and 21.1 kg CO_2 per dollar of GDP, respectively) are much greater than in the most developed countries (e.g., 5.2, 4.5, and 3.8 kg CO_2 per dollar of GDP in the United States, Europe, and Japan, respectively; Fig. 2C), showing that the infrastructural inertia of emissions is greatest where industrialization is under way but incomplete.

Warming and atmospheric CO_2 concentrations from committed emissions were calculated using version 2.9 of the University of Victoria Earth System Climate Model, an intermediate-complexity coupled climate-carbon model (*25*, *26*). We used specified historical CO_2 concentrations to simulate the period from 1750 to 2010. From 2010 to 2100, we specified CO_2 emissions according to our estimates of infrastructural commitments and, in some cases, CO_2 emissions from non-energy sources. Global mean temperatures increase less than 1.4°C in all scenarios, stabilizing when fossil fuel emissions approach zero around mid-century (Fig. 1D). At the upper bound of estimated emissions, the atmospheric concentration of CO_2 peaks in 2046 at 427 ppm (Fig. 1C).

If existing energy infrastructure (e.g., power plants, motor vehicles, furnaces) was used for its normal life span and no new devices were built that emitted CO_2, atmospheric concentrations of CO_2 would peak below 430 ppm and future warming would be less than 0.7°C. However, there is little doubt that more CO_2-emitting devices will be built. Our analysis considers only devices that emit CO_2 directly. Substantial infrastructure also exists to produce and facilitate use of these devices. For example, factories that produce internal combustion engines, highway networks dotted with gasoline refueling stations, and oil refineries all promote the continuation of oil-based road transport emissions. Moreover, satisfying growing demand for energy without producing CO_2 emissions will require truly extraordinary development and deployment of carbon-free sources of energy, perhaps 30 TW by 2050 (*27*, *28*). Yet avoiding key impacts of climate change depends on the success of efforts to overcome infrastructural inertia and commission a new generation of devices that can provide energy and transport services without releasing CO_2 to the atmosphere.

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Supporting Online Material

www.sciencemag.org/cgi/content/full/329/5997/1330/DC1
Materials and Methods
Figs. S1 to S3
Tables S1 and S2
References

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Stable Isotope Measurements of Martian Atmospheric CO_2 at the Phoenix Landing Site

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Carbon dioxide is a primary component of the martian atmosphere and reacts readily with water and silicate rocks. Thus, the stable isotopic composition of CO_2 can reveal much about the history of volatiles on the planet. The Mars Phoenix spacecraft measurements of carbon isotopes [referenced to the Vienna Pee Dee belemnite (VPDB)] [$\delta^{13}C_{VPDB} = -2.5 \pm 4.3$ per mil (‰)] and oxygen isotopes [referenced to the Vienna standard mean ocean water (VSMOW)] ($\delta^{18}O_{VSMOW} = 31.0 \pm 5.7$‰), reported here, indicate that CO_2 is heavily influenced by modern volcanic degassing and equilibration with liquid water. When combined with data from the martian meteorites, a general model can be constructed that constrains the history of water, volcanism, atmospheric evolution, and weathering on Mars. This suggests that low-temperature water-rock interaction has been dominant throughout martian history, carbonate formation is active and ongoing, and recent volcanic degassing has played a substantial role in the composition of the modern atmosphere.

Carbon dioxide (CO_2) is the dominant gas in the martian atmosphere, and its stable isotopic composition can provide constraints on Mars volatile reservoirs, carbon cycle, and climate history. CO_2 is involved in many major planetary processes that affect volatile reservoirs of the planet's surface, including volcanic degassing, atmospheric loss, and rock weathering and carbonate formation. Additionally, CO_2 rapidly equilibrates with water, and the oxygen isotopic composition of CO_2 may provide insight into the action of liquid water at the planet's surface. Stable isotopes are effective tracers of the history of CO_2 because they are fractionated in predictable ways by each geological process. Thus, the stable isotopic composition of the atmospheric CO_2 of Mars will record the sum of the geologic processes in which it has participated, making it possible to quantifiably constrain them.

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Previous measurements on the surface of Mars of the isotopic composition of atmospheric CO_2 have lacked sufficient precision to be useful for meaningful interpretation (Table 1). Measurements of trapped CO_2 gas in martian meteorite EETA 79001 impact glass claimed higher precision and showed elevated $\delta^{13}C$ values (Table 1), supporting a hypothesis suggesting that the modern martian atmosphere was enriched in ^{13}C (*1*). However, more recent Earth-based spectroscopic measurements of the martian atmosphere have measured the martian CO_2 to be depleted in ^{13}C relative to CO_2 in the terrestrial atmosphere (*2*).

Here, we report high-precision measurements, made at the surface of Mars, of atmospheric CO_2. The Thermal and Evolved Gas Analyzer (TEGA) instrument on the Mars Phoenix Lander (*3*) included a magnetic-sector mass spectrometer (EGA) (*4*), which had a goal of measuring the isotopic composition of martian atmospheric CO_2 to within 0.5%. Its counting rates were averaged over ~5-min increments for masses 44, 45, and 46. These masses include all of the major stable isotopes of carbon (^{12}C and ^{13}C) and oxygen (^{16}O, ^{17}O and ^{18}O) and are universally used to make isotopic measurements of CO_2 in terrestrial laboratories. Isotope ratios were calculated from these averages and were corrected for the deadtime in the preamplifier discriminator circuit (fig. S1), the background measured in the instrument before ingesting gas, and the $^{12}C^{17}O^{16}O$ contribution to mass 45. The correction for ^{17}O contribution is relatively small as compared with our uncertainties because of the extremely low abundance of ^{17}O in the solar system. Therefore, only unrealistically large uncertainties in the martian $\delta^{17}O$ value [>60 per mil (‰)] could affect the magnitude of our uncertainties. Finally, the corrected isotope ratios were calibrated by referencing analyses of a CO_2 gas of known composition carried to Mars on the lander (Fig. 1) (*5*).

The Phoenix results (Table 1) show that the carbon isotopic composition of martian atmospheric CO_2 is not enriched in ^{13}C, which is in agreement with (*2*), and are within the uncertainty of most previous isotopic measurements (Fig. 2). The $\delta^{18}O$ referenced to the Vienna standard mean ocean water (VSMOW) ($\delta^{18}O_{VSMOW}$) value of martian atmospheric CO_2 (31.0‰) is lighter than terrestrial atmospheric CO_2 (41‰), whereas the $\delta^{13}C$ referenced to the Vienna Pee Dee belemnite (VPDB) ($\delta^{13}C_{VPDB}$) (–2.5‰) is similar to terrestrial atmospheric CO_2 (–7‰). However, this result for carbon is in contradiction with values reported from trapped gases in impact glass from EETA 79001 (*1*), which measured CO_2 that was more enriched in ^{13}C. It is possible that this trapped CO_2 was derived from the impact volatilization of carbonates that were enriched in ^{13}C. This is indicated by the presence of martian carbonates elsewhere in EETA 79001, and the suggestion that the impact glass from which the gas measurements were made may include a martian regolith component (*6*), which probably contained 2 to 3% carbonate (*3*).

Carbonates in martian meteorites preserve the carbon and oxygen isotopic composition of the CO_2 from which they formed and provide an opportunity to look back into time to evaluate the history of carbon and H_2O on the planet. On Earth, carbonates are typically fractionated in both carbon and oxygen from both CO_2 and water. The $\delta^{13}C$ of terrestrial CO_2 averages around –7‰, which is very similar to magmatic CO_2

Table 1. All published measurements of the isotopic composition of martian atmospheric CO_2, including results from this study (*1*, *2*, *28*–*32*). Uncertainties for the Phoenix measurements are calculated as SE from the 2σ SD of all of the measurements. GC, gas chromatograph; MS, mass spectrometer.

	Carbon		Oxygen		
	$^{13}C/^{12}C$ (uncertainty)	$\delta^{13}C_{VPDB}$ (uncertainty) (‰)	$^{18}O/^{16}O$ (uncertainty)	$\delta^{18}O_{VSMOW}$ (uncertainty) (‰)	Reference
SNC-trapped gas (EETA79001)	0.0116 (0.0001)	36 (10)			(*1*)
Viking, neutral MS	0.0111 (0.0007)	–10 (58)	0.00204 (0.00011)	18 (55)	(*28*)
Viking, GC MS	0.0112 (0.0006)	0 (50)	0.00201 (0.00010)	0 (50)	(*29*)
Spectroscopy	0.0104 (0.0007)	–73 (58)	0.00193 (0.00024)	–40 (120)	(*30*)
Spectroscopy	0.0106 (0.0017)	–60 (150)			(*31*)
Spectroscopy	0.0112 (0.0012)	0 (110)			(*32*)
Spectroscopy	0.0110 (0.0002)	–22 (20)	0.00204 (0.00004)	18 (18)	(*2*)
Phoenix MS	0.01120 (0.00005)	–2.5 (4.3)	0.002067 (0.000011)	31.0 (5.7)	(this study)

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(*7*). The $\delta^{18}O$ averages ~41‰ and is strongly influenced by low-temperature equilibration with seawater ($\delta^{18}O = 0$‰), which has a fractionation factor of ~40‰ at 25°C (*7*). Terrestrial carbonates in equilibrium with these reservoirs at 25°C would have $\delta^{13}C \sim 3$‰ and $\delta^{18}O \sim 29$‰ (*7*). Variations in these isotopic values can yield valuable information regarding the influence of biological processes, temperatures of formation, and other details of the carbonate formation environment.

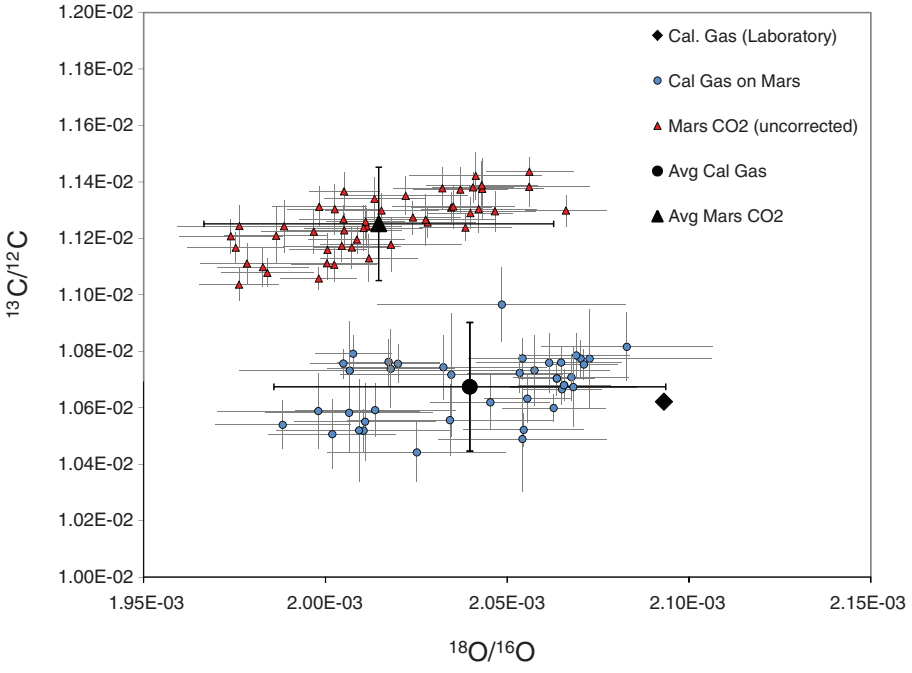

Fig. 1. Corrected but uncalibrated isotope ratios of measurements performed at the martian surface by the TEGA instrument. Small triangles are individual ~5-min measurements of martian atmospheric CO_2 that have not yet been calibrated by results from calibration gas measurements. Small circles are corrected measurements of calibration gas. Larger triangle and circle are averages showing 2σ SD. These are also plotted with results from the laboratory measurement of the TEGA calibration gas before flight. Data are listed in Table 1 and in (*5*).

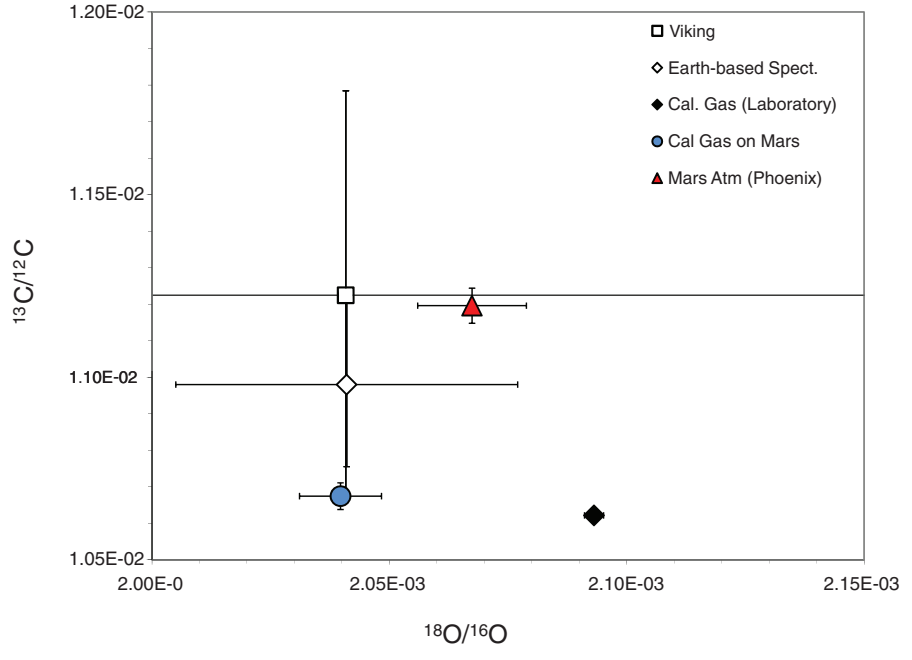

Fig. 2. Corrected and calibrated results of martian atmospheric CO_2 measurement plotted next to results from Viking lander (*28*, *29*), Earth-based spectroscopy (*2*), and measurements of calibration gas on Earth and Mars. The result for calibration gas on Mars is the uncalibrated value to show the magnitude of the calibration correction. Error bars on TEGA measurements are 2σ SE.

Unfortunately, $\delta^{13}C$ measurements from acid extractions and thermal analyses of martian meteorites range from 65‰ to –20‰, revealing substantial variability that has been very difficult to understand (*8*–*15*). Much of these data come from three martian meteorites that each sample alteration events from different periods of martian history: ALH 84001 (<4 billion years ago) (*16*), Nakhla (<600 million years ago) (*17*), and EETA 79001 (<200 million years ago) (*18*). A large hindrance for interpreting these data has been a lack of information about the isotopic composition of larger reservoirs on Mars.

ALH 84001 contains carbonates that have been dated to 3.9 billion years ago and are generally enriched in ^{13}C (*14*, *16*). This signature is likely to be originally derived from the ancient martian atmospheric CO_2 that had been enriched in ^{13}C by early atmospheric loss processes (*19*). In situ ion microprobe measurements of the $\delta^{13}C_{VPDB}$ of ALH 84001 carbonates range from 30‰ to 65‰, with $\delta^{18}O_{VSMOW}$ ion microprobe measurements ranging from –10‰ to 25‰ (*20*, *21*). Isotope measurements of CO_2 extracted by phosphoric acid generally agree with these measurements but also indicate the presence of a lighter carbon component with $\delta^{13}C$ near 10‰ (Fig. 3).

Nakhla carbonates are in general less abundant than ALH 84001 carbonates, and the aqueous alteration event has been dated to be ~600 million years old (*17*). Phosphoric acid measurements show a similar pattern to ALH 84001 measurements, with some measurements showing very enriched $\delta^{13}C$ values near 40‰ and other measurements clustering around 10‰ (*10*, *14*).

EETA 79001 is a Shergottite that features a "white druse" material that has been suggested to be martian in origin on the basis of petrologic arguments (*22*); isotopic measurements of this material result in a $\delta^{13}C_{VPDB}$ near 8‰ and a $\delta^{18}O_{VSMOW}$ near 22‰ (*12*, *15*). These isotopic values have an oxygen isotope composition that is too enriched for Antarctic weathering, which features waters extremely depleted in ^{18}O (*15*, *23*).

When all of the published carbonate analyses are plotted next to the Phoenix results, they reveal a pattern that suggests a potential 4-billion-year history of H_2O and CO_2 on Mars (Fig. 3). This history is dominated by three components: modern martian atmosphere, early martian atmosphere, and magmatic CO_2.

The modern atmosphere is recorded by carbonates in the 200-million-year-old martian meteorite EETA 79001. The isotopic composition of these carbonates is consistent with formation at low temperatures (~0 to 25°C) from the modern martian atmosphere measured by Phoenix (Fig. 3). In addition, some carbonate measurements in Nakhla, Governor Valadares, and ALH 84001 are also in this range, suggesting that these meteorites also contain a modern carbonate component.

The ancient atmosphere of Mars is likewise recorded in carbonates from the oldest martian meteorite ALH 84001. The average carbon and

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oxygen isotopic composition of the carbonates in ALH 84001 suggest an ancient atmospheric composition enriched in $\delta^{13}C$ but of similar $\delta^{18}O$ content to the modern atmosphere (*24*). These isotope values are more widely scattered because of large heterogeneities within the meteorite itself (*20*, *21*). Careful ion microprobe analyses have shown the values to follow a covariant trend, possibly reflecting kinetic fractionation processes that were active during their precipitation (*20*).

Magmatic CO_2 appears to be preserved in the martian meteorite Zagami. Phosphoric acid CO_2 extractions of Zagami (*10*) show a mixing line between modern martian CO_2 and a component with $\delta^{13}C$ of –20 to –30‰ and $\delta^{18}O$ of ~10‰ (Fig. 3). This is consistent with thermal analyses of martian meteorites (*25*) and theoretical high-temperature equilibrium between silicate rocks and CO_2 (*15*).

All of these measurements can be synthesized into a model that broadly constrains the history of water, volcanism, atmospheric development, and water-rock interaction on Mars. In this model, early atmospheric CO_2 was enriched in ^{13}C through early sputtering and hydrodynamic escape (*25*, *26*). This early enrichment has since been removed over the course of history (Fig. 3) through carbonate formation and dilution from mantle degassing that outweighed ongoing atmospheric loss. This suggests that atmospheric loss processes were important early in martian history but have been less important since that time, whereas volcanic degassing still plays a substantial role. Thus, on the basis of the carbon isotopes it is unlikely that the somewhat enriched $\delta^{18}O$ values for the modern CO_2 are due to fractionation stemming from atmospheric loss processes. Carbonate formation is an important factor in removing ^{13}C from the atmosphere, and indications of modern carbonate formation in many of the martian meteorites (Fig. 3) suggests that carbonate formation is a substantial ongoing process in the current martian environment, which conflicts with the widely held belief that aqueous environments on modern Mars are largely acidic.

The model also calls for the oxygen isotope composition of CO_2 to be buffered by surficial reservoirs of water or ice (*23*), which in turn were buffered by substantial early water-rock interaction. This composition has remained similar through time, as indicated by the carbonate record (Fig. 3). The average oxygen isotope composition ($\delta^{18}O \approx 19‰$) of the ancient ALH 84001 carbonates (*14*) is similar to the oxygen isotopic composition of the modern carbonates in EETA 79001 ($\delta^{18}O \approx 21‰$) (*12*, *15*). This could be the result of substantial ongoing water-rock interaction, indicating an active low-temperature hydrology on Mars throughout its history (*19*) and would contradict the commonly held view that aqueous activity has been very limited on Mars for the past 2 to 3 billion years. Another possibility to explain the oxygen isotope record is that the current water reservoir on Mars is very large as compared with magmatic degassing and atmospheric loss since the end of the early Noachian. This extensive reservoir could then buffer the oxygen isotopic composition of water and CO_2 through time (*19*), even if the total amount of water-rock interaction has been limited through much of the planet's history.

The oxygen isotope composition of martian atmospheric CO_2 is enriched in ^{18}O ($\delta^{18}O = 31.0 \pm 5.7‰$) when compared with that of the silicates on Mars ($\delta^{18}O = 4.2$). This is substantially different from magmatic CO_2, which would be in high-temperature equilibrium with the rocks and have a $\delta^{18}O$ near 8‰ (*15*). Similar to terrestrial CO_2, the most likely explanation for this isotopic enrichment is through low-temperature isotopic exchange with liquid water in which the fractionation of oxygen isotopes strongly enriches CO_2 in ^{18}O. If this equilibration took place at an average temperature of 0°C, the $\delta^{18}O$ of liquid water would be close to –15‰ (*15*). CO_2 and H_2O may also exchange oxygen via photochemical reactions in the atmosphere; however, fractionations attributable to this mechanism are unknown. Therefore, if photochemical reactions dominate over aqueous reactions then the $\delta^{18}O$ of the water on Mars may be very different. However, aqueous reactions probably dominate, given that both martian atmospheric CO_2 and carbonates in EETA 79001 have $\delta^{18}O$ values that are consistent with H_2O, with a $\delta^{18}O$ near –15‰.

Previous estimates of the $\delta^{18}O$ of water on Mars have relied on a model described by Clayton and Mayeda (*15*), in which water and CO_2 equilibrate with silicate rocks at high temperature during initial outgassing and then equilibrate at low temperature with no further interaction with the silicate crust. In this model, $\delta^{18}O$ values of both water and CO_2 are strongly dependent on the ratio of H_2O/CO_2. The recent discoveries by Mars Express and the Mars Reconnaissance Orbiter that the ancient crust of Mars contains substantial weathering products suggest that the assumption of no further interaction with the silicate crust after initial outgassing is invalid. Thus, the $\delta^{18}O$ of water on Mars was and may continue to be buffered by exchange with the silicate crust.

The average $\delta^{18}O$ of water present on early Mars can be independently calculated assuming it is buffered by low-temperature (0 to 25°C) water-rock interaction with a fractionation of 20‰ (*27*). The $\delta^{18}O$ of the water would be ~–16‰, which is nearly identical to $\delta^{18}O$ of water calculated from the Phoenix results. If this water-rock interaction had primarily occurred at higher temperatures, then it would probably have resulted in water with $\delta^{18}O$ close to that of terrestrial oceans (*27*), which have a $\delta^{18}O$ near 0‰ and are strongly influenced by high-temperature water-rock interaction at mid-ocean ridges. If the water in equilibrium with martian atmospheric CO_2 does represent average water on the martian surface, then the preponderance of water-rock interaction on Mars took place at low temperatures, indicating that the extensive phyllosilicate exposures in the ancient crust were predominately formed at low temperatures. This is consistent with a lack of plate

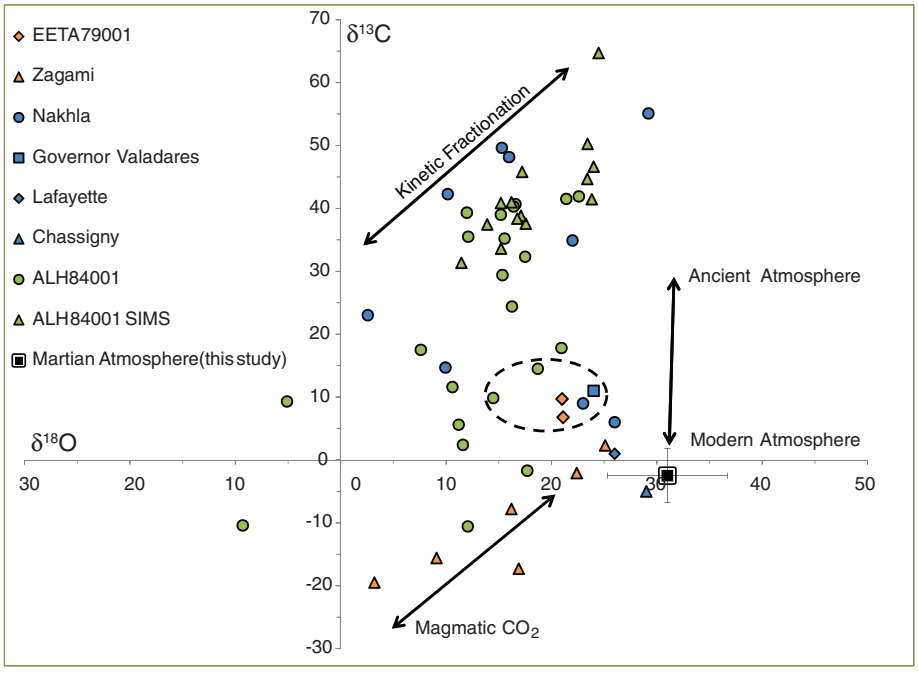

Fig. 3. Carbon and oxygen isotope measurements of martian meteorite carbonates. All measurements (except where noted) are results from phosphoric acid treatment of meteorites at a variety of temperatures (*8*, *10*–*15*). The ALH 84001 SIMS data are a combination of in situ carbon (*20*) and oxygen (*21*) data by use of Mg content to correlate the two data sets. Arrows indicate probable sources for isotope variation within the diagram, as discussed in the text. The dashed oval represents the equilibrium composition of carbonates that could form from the modern martian atmosphere measured in this study.

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tectonics and a lack of substantial hydrothermal systems on early Mars.

Biological processes strongly fractionate carbon isotopes, typically incorporating a larger proportion of ^{12}C than is present in the CO_2 reservoir in which they live. On a global scale, biological processes should preferentially remove ^{12}C and store it in organic matter, increasing the $\delta^{13}C$ of the remaining CO_2 reservoir. This process is one of many that may be operating on Mars; thus, the atmospheric measurement reported here does not provide a means for unambiguous detection of biological processes. Instead, this measurement clarifies the characteristics of major carbon and oxygen isotope reservoirs on Mars.

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Planar Cell Polarity Acts Through Septins to Control Collective Cell Movement and Ciliogenesis

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The planar cell polarity (PCP) signaling pathway governs collective cell movements during vertebrate embryogenesis, and certain PCP proteins are also implicated in the assembly of cilia. The septins are cytoskeletal proteins controlling behaviors such as cell division and migration. Here, we identified control of septin localization by the PCP protein Fritz as a crucial control point for both collective cell movement and ciliogenesis in *Xenopus* embryos. We also linked mutations in human Fritz to Bardet-Biedl and Meckel-Gruber syndromes, a notable link given that other genes mutated in these syndromes also influence collective cell movement and ciliogenesis. These findings shed light on the mechanisms by which fundamental cellular machinery, such as the cytoskeleton, is regulated during embryonic development and human disease.

A major unresolved question in embryonic tissue morphogenesis concerns how developmental signals are translated into changes in cell behavior (*1*). As cells become specified, different cell types initiate specific, yet varied, behaviors. For example, cells in the notochord and spinal cord of vertebrates interdigitate in a planar polarized manner forming a longer, narrower array (*2*, *3*). This collective cell movement, convergent extension (CE), drives gastrulation and elongates the embryonic axis (Fig. 1A) (*4*–*7*). By contrast, multiciliated epithelial cells undergo a radical process of cellular morphogenesis, developing dozens of apical motile cilia (*8*, *9*). Proteins in the Wnt/ PCP pathway act in both cell types (*6*, *7*, *10*–*18*), but how they regulate such dissimilar cellular behaviors remains unknown.

We investigated the vertebrate ortholog of the cytoplasmic WD40 repeat protein Fritz, which controls PCP in *Drosophila* (*19*). We first assessed the requirement for Fritz in *Xenopus* gastrulation, where PCP-mediated CE in the dorsal mesoderm drives the reorganization of the germ layers and closure of the blastopore. (Fig. 1A) (*2*, *4*, *6*, *20*). *Fritz* was strongly expressed in these cells, and morpholino (MO)–mediated knockdown elicited defective gastrulation indicated by a persistent open blastopore and failure of axis elongation (Fig. 1, B to D, and H; and fig. S1, A and E to I).

We then explored the cell behavioral basis of these defects using explanted gastrula tissue in organotypic culture ("Keller" explants) (fig. S2) (*2*, *10*). During normal CE, cells polarize and align their long axes mediolaterally, acquiring elongate morphologies as they interdigitate (Fig. 1, A and I, and fig. S2). Core PCP proteins govern both polarized alignment and cell elongation

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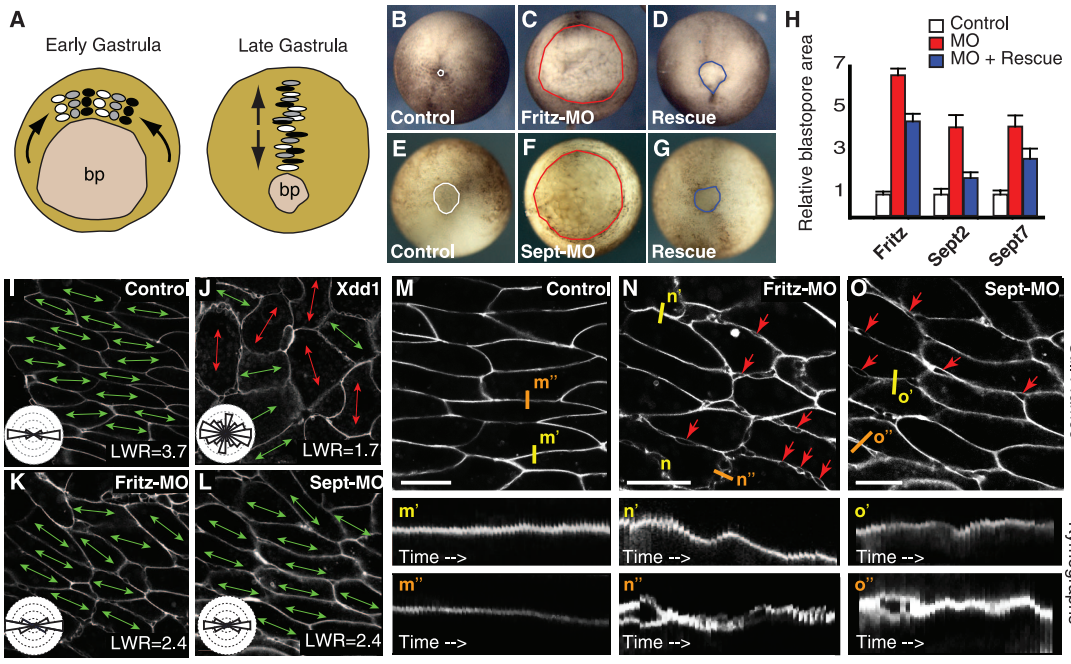

Fig. 1. Fritz and Septins control convergent extension. (**A**) Cell intercalation (black, white, and gray cells) drives CE, elongating the body axis and closing the blastopore (bp) during gastrulation. (**B**) Control embryo with closed blastopore (white circle). (**C**) Sibling Fritz morphants fail to close the blastopore (red). (**D**) Coinjection of GFP-Fritz mRNA rescued blastopore closure (blue). (**E**) Control embryo. (**F**) Sibling sept7 morphants fail to close the blastopore (red). (**G**) Sept7 mRNA rescues closure of blastopore (blue). (**H**) Quantification of blastopore closure (mean ± SEM; *n* values for each column, left to right, are as follows: 21, 20, 28, 18, 11, 8, 16, 12, and 18). (**I**) Still frame from movie of control Keller explant; green arrows indicate mediolaterally aligned cells, alignment of all cells is quantified in the inset diagram. (**J**) Xdd1, a PCP-specific dominant-negative Dishevelled, disrupts elongation and alignment (red arrows indicate misoriented cells). (**K**) Fritz morphant cells display defective elongation, but normal polarized alignment. (**L**) Sept2 morphant cells display defective elongation, but normal polarized alignment. (**M**) Control cells (movie 1); orange/yellow lines indicate positions of kymographs in **m′** and **m″**. (**N**) Fritz morphant Keller explant; red arrows indicate intercellular spaces (movie 2). (**O**) Sept2 morphant Keller explant; red arrows indicate intercellular spaces (movie 3).

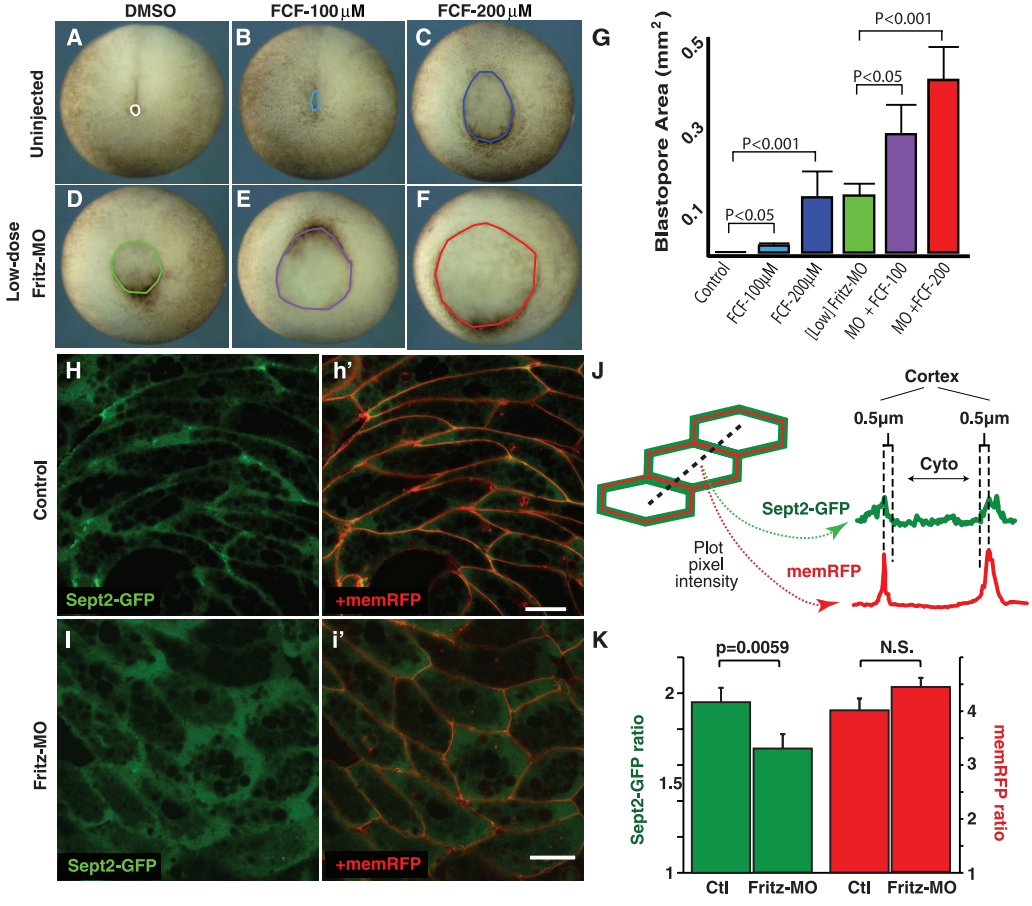

Fig. 2. Functional interaction between Fritz and septins. (**A**) Control embryo with closed blastopore. (**B**) Sibling embryo treated with 100 μM FCF. (**C**) Sibling treated with 200μM FCF. (**D**) Sibling injected with a low dose of Fritz MO. (**E**) Sibling Fritz morphant treated with 100μM FCF. (**F**) Sibling Fritz morphant treated with 200 μM FCF. (**G**) Quantification of blastopore closure (mean ± SEM; *n* = nine embryos per column). (**H**) Sept2-GFP concentrated at the cortex (red in h′) of cells engaged in CE. (**I**) Cortical sept2-GFP concentration was reduced in Fritz morphants. (**J**) Sept2-GFP localization was quantified as the ratio of cortical versus cytoplasmic pixel intensities. (**K**) Cortical/cytoplasmic Sept2-GFP ratio was reduced significantly in Fritz morphants; the ratio of coexpressed membrane-RFP is unchanged (mean ± SEM; *n* = 123 cells for control, 150 for morphant).

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(Fig. 1J, and fig. S3) (*10*, *12*). By contrast, Fritz morphant cells displayed significantly reduced cell elongation, whereas their polarized alignment was largely normal (Fig. 1K, and fig. S3). Moreover, in time-lapse movies, cell membranes in controls were relatively static, whereas Fritz morphant cell membranes undulated, frequently producing intercellular spaces that opened and closed rapidly between cells (Fig. 1, M and N, and movies S1 and S2). Thus, Fritz controls cell shape but not polarization during CE and thus executes a specific subset of PCP-mediated cell behaviors in *Xenopus*, consistent with data from *Drosophila* (*19*).

The instability of plasma membranes in Fritz morphants suggested a possible role for septins, as these cytoskeletal elements can brace plasma membranes and resist aberrant cell shape deformation (*21*–*23*). Sept2 and sept7 were expressed strongly in cells during CE, and MO-mediated knockdown of either resulted in defective gastrulation (Fig. 1, E to H, and fig. S4). A cell-permeable inhibitor of septin dynamics, forchlorfenuron (FCF) (*24*, *25*), also elicited gastrulation defects (Fig. 2, A to C and G). Moreover, cells in septin morphants displayed reduced cell elongation but normal polarization, similar to Fritz morphants (Fig. 1L and fig. S3). Finally, time-lapse imaging revealed membrane undulations in septin morphants similar to those in Fritz morphants (Fig. 1O, movies S3 and S4, and fig. S5).

These similar phenotypes led us to test for functional interactions between Fritz and septins. First, application of FCF exacerbated significantly the gastrulation defects in low-dose Fritz morphants (Fig. 2, D to G). Second, sept2 was associated consistently with Fritz in coimmunoprecipitations from *Xenopus* embryos (fig. S6). Finally, septins act at the cortex in cultured cells (*22*, *23*), and both sept2 fused to green fluorescent protein (sept2-GFP) and Fritz-GFP were concentrated at the cell cortex during CE (Fig. 2H and fig. S1J). Moreover, the ratio of cortical-to-cytoplasmic sept2-GFP was consistently reduced in Fritz morphants compared with controls (Fig. 2, I to K). These data suggest that Fritz and septins collaborate during PCP-mediated collective cell movements.

In addition to their role in CE, vertebrate orthologs of certain *Drosophila* PCP proteins control ciliogenesis (*13*–*18*). At organogenesis stages, *Fritz* was expressed in ciliated cell types, and Fritz morphants displayed defects in craniofacial morphogenesis and Hedgehog signaling similar to those associated with defective ciliogenesis (Fig. 3, A to F, and fig. S1, J to L) (*13*). Exploiting the multiciliated cells of the *Xenopus* epidermis (Fig. 3, G and H) (*9*, *13*, *15*, *16*), we found that those lacking Fritz (Fritz knockdown) resulted in the development of fewer and shorter cilia (Fig. 3, G and H).

No common mechanism as yet explains the role of PCP proteins in ciliogenesis and collective cell movement, but because Fritz functions with septins during CE, we tested the possibility that these proteins also act together during ciliogenesis. Indeed, sept7 and Fritz were localized along ciliary axonemes and in distinct foci near basal bodies (Fig. 3, I and J, and fig. S1, J and K). These sept7 foci were most prominent, and frequently appeared ringlike, in single optical sections of the apical surface of a multiciliated cell viewed en face (Fig. 3I, inset). These sept7 structures were consistent with the septin-based diffusion barrier at the base of cilia (*26*, *27*) and also consistent in size with septin-based rings that self-assemble in vitro (*28*).

In Fritz morphants, disrupted ciliogenesis was associated with defects in the size and shape of

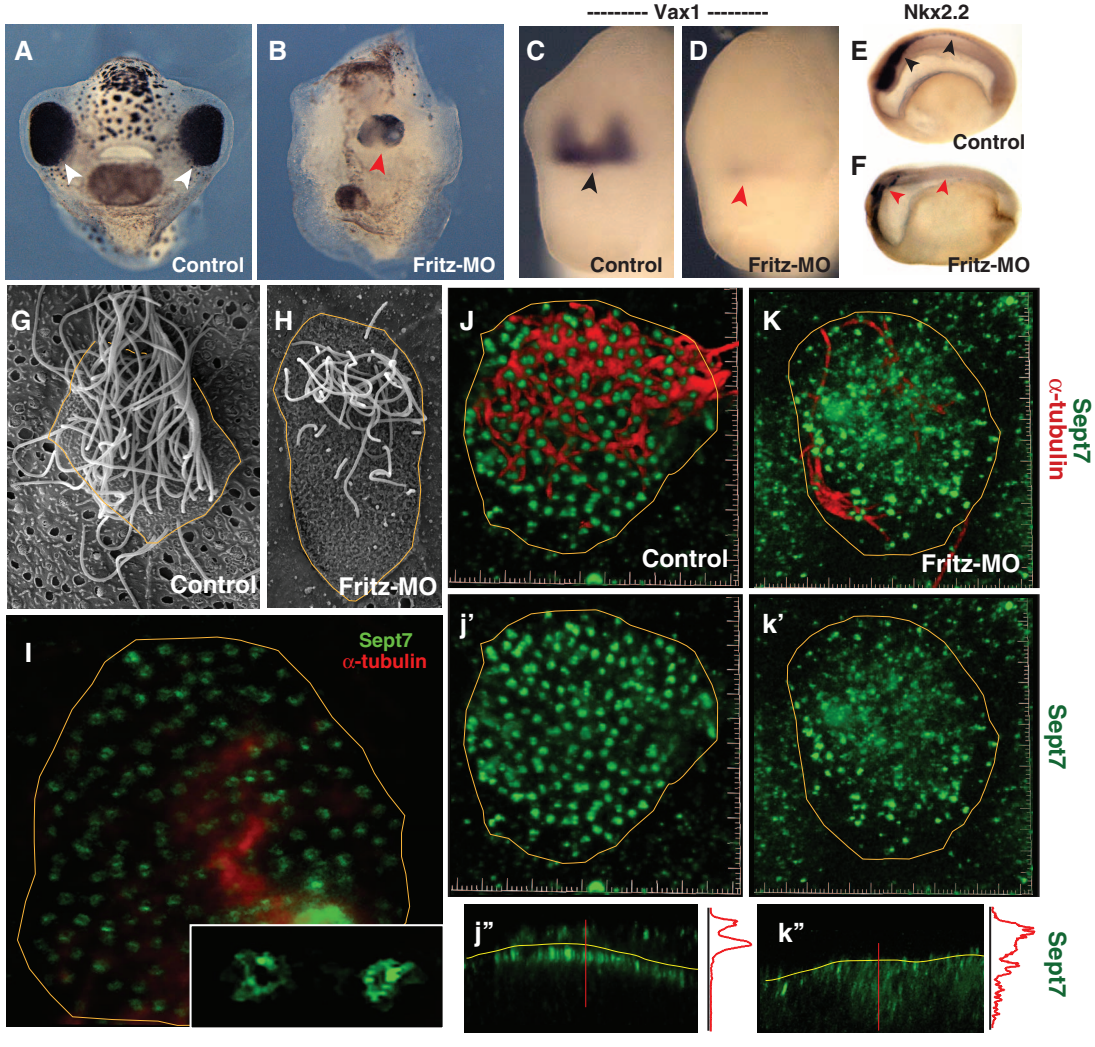

Fig. 3. Fritz controls septin localization, ciliogenesis, and Hedgehog signaling. (**A**) Control tadpole (anterior view; arrowheads indicate eyes). (**B**) Sibling Fritz morphant (red arrowhead indicates single, medial eye). (**C**) *Vax1* expression in control embryo. (**D**) *Vax1* expression is lost in a Fritz morphant. (**E**) Sagittal view of *Nkx2.2* expression in the spinal cord of a control embryo, black arrowheads. (**F**) *Nkx2.2* expression is lost in Fritz morphant, red arrowheads. (**G**) A single multiciliated cell from the *Xenopus* epidermis. (**H**) Multiciliated cells in Fritz morphants display fewer and shorter cilia. (**I**) Sept7 in ring-like structures (inset) at the base of cilia in a confocal slice of a multiciliated cell. (**J**) Sept7 structures (green; **j'**) are highly ordered in a stack from a control multiciliated cell: cilia are visible in red. (**K**) Sept7 structures (green; **k'**) are disorganized in a Fritz morphant multiciliated cell: few cilia are visible in red. (**j"**) Z-projection reveals tight association of Sept7 with the apical surface (yellow line); intensity plot is shown at right (red line). (**k"**) Z-projection reveals loss of sept7 from the apical surface.

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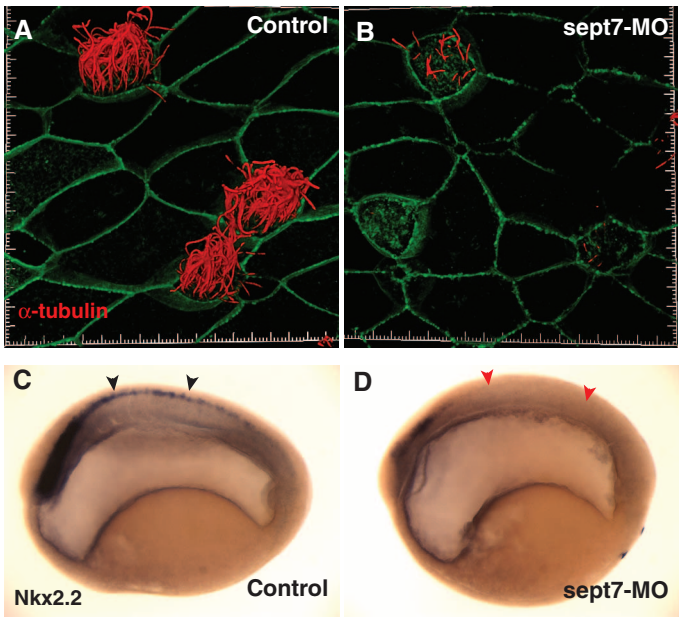

Fig. 4. Septins govern ciliogenesis and Hedgehog signaling in developing embryos. (**A**) Control *Xenopus* multiciliated cells (**B**) Cilia are shorter and fewer in number sept7 morphants (**C**) Sagittal view of the Hedgehog target gene *Nkx2.2* in the spinal cord of a control embryo marked by black arrowheads. (**D**) *Nkx2.2* expression is lost in sept2 and sept7 morphant embryos; red arrowheads. (**E**) Table of mutations in human Fritz (C2ORF86) in BBS and MKS patients. In only two cases (*, **) were mutations present in trans with mutations in a known BBS- or MKS-associated gene.

E **Summary of Fritz candidate pathogenic alleles**

Individual	Clinical Diagnosis	C2ORF86 Allele 1	C2ORF86 Allele 2	Other Mutations
AR248	BBS	c.76-1G>t	c.76-1G>t	-
AR316	BBS	L208F	wt	BBS12*
MR-1	BBS	S708F	wt	-
MKS142	MKS	R55K	wt	MKS6**
MKS79	MKS	F13L	wt	-

* c.1092delA, htz; c.2133G>C, htz
**c.3522_3523insTG, htz; c.4496+2 T>A, htz

individual sept7 structures, as well as their positioning at the apical surface (Fig. 3, J and K). The mean area of Sept7 structures in Fritz morphant multiciliated cells was reduced significantly compared with controls (fig. S7A), and individual sept7 structures displayed heterogeneous pixel intensities in Fritz morphants, which suggested a defect in their structure (fig. S7B). Finally, both sept7 and sept2 were restricted to the apical surface and axonemes of control multiciliated cells but were detected consistently throughout the cytoplasm of Fritz morphant cells (Fig. 3, j″ and k″, and fig. S8, A to D). Consistent with a link between Fritz, septins, and ciliogenesis, knockdown of Sept7 or Sept2 elicited defects in ciliogenesis (Fig. 4, A and B, and fig. S8, E and F). Finally, septin knockdown also disrupted expression of Hedgehog target genes in the midline, although Notch targets were unaffected (Fig. 4, C and D, and figs. S8, G and H, and S9).

Fritz thus acts together with septins to control both CE and ciliogenesis in *Xenopus*. Human genes associated with Meckel-Gruber (MKS) and Bardet-Biedl (BBS) syndromes likewise affect both processes (*29*–*32*), so we asked whether mutations in Fritz might contribute to these disorders. We found a significant enrichment of nonsynonymous coding changes in human Fritz (C2orf86) in MKS and BBS patients as compared with controls (6 alleles in 192 patients vs. 0 in 384 controls; $P < 0.015$; Fig. 4E and fig. S10A). In the MKS cohort, we did not identify alleles sufficient to explain the phenotype, which suggested that these changes might interact in trans with primary MKS loci [e.g., (*30*, *33*)]. For the BBS cohort, we found two heterozygous missense alleles that were absent from 384 ethnically matched controls, HapMap, and 1000 genomes. Also, two of these changes map to the same surface-exposed face of the predicted β-propeller structure of the Fritz protein (fig. S10, B and C).

Notably, we also found a homozygous Fritz mutation that segregated with the disorder in a BBS family (Fig. 4E). Both parents and an unaffected sib are heterozygous carriers (fig. S10D), and this position is invariant in Fritz, absent from 384 controls, HapMap, and 1000 genomes. Although we are cautious in interpreting data from a single family, this result suggests that Fritz loss-of-function mutations may be sufficient to cause BBS, and corroborates other studies linking BBS proteins to ciliogenesis and CE (*29*–*32*).

Here, we link Fritz to the septin cytoskeleton in both ciliogenesis and collective cell movement to provide insights into both PCP signaling and the function and regulation of septins during vertebrate embryogenesis. An important challenge will be to understand the broader protein network underlying Fritz-dependent septin functions in vivo. Intriguing candidates are the previously identified BBS and MKS proteins and also IFT88, as these proteins are implicated in both ciliogenesis and CE (*29*, *34*).

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Self-Assembly of Filopodia-Like Structures on Supported Lipid Bilayers

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Filopodia are finger-like protrusive structures, containing actin bundles. By incubating frog egg extracts with supported lipid bilayers containing phosphatidylinositol 4,5 bisphosphate, we have reconstituted the assembly of filopodia-like structures (FLSs). The actin assembles into parallel bundles, and known filopodial components localize to the tip and shaft. The filopodia tip complexes self-organize—they are not templated by preexisting membrane microdomains. The F-BAR domain protein toca-1 recruits N-WASP, followed by the Arp2/3 complex and actin. Elongation proteins, Diaphanous-related formin, VASP, and fascin are recruited subsequently. Although the Arp2/3 complex is required for FLS initiation, it is not essential for elongation, which involves formins. We propose that filopodia form via clustering of Arp2/3 complex activators, self-assembly of filopodial tip complexes on the membrane, and outgrowth of actin bundles.

Actin assembly is largely responsible for cell shape and movement in eukaryotic cells (*1*). Actin filaments underlie a range of morphological structures; among these, filopodia, which contain closely apposed bundled parallel actin filaments, are of particular interest (*2*, *3*). They have numerous biological roles, but their mechanism of formation is poorly understood. The persistence of actin growth in a parallel bundle in filopodia suggests roles for proteins with anti-capping and/or processive elongation activity [such as vasodilator-stimulated phosphoprotein (VASP) and formins] (*4*–*8*). But formins are also important in lamellipodia (*9*). The role of the Neural Wiskott-Aldrich syndrome protein (N-WASP)/Arp2/3 complex pathway in filopodia formation is also contentious (*8*, *10*–*14*). Although there are in vitro models of actin bundling (*15*–*17*), no current experimental system recapitulates two physiological aspects of filopodia: (i) spontaneous formation of actin bundles in the presence of capping activity and (ii) the assembly of a membrane-localized tip complex.

To investigate actin polymerization at membranes and to exploit advanced microscopic techniques like total internal reflection fluorescence (TIRF) microscopy, we have replaced liposomes as the source of lipids with supported lipid bilayers (*18*). Purified Cdc42.GTPγS, N-WASP-WIP, toca-1, Arp2/3 complex, and actin comprise a minimal set of proteins for stimulation of actin nucleation by $PI(4,5)P_2$-containing liposomes in vitro (*19*). When these proteins are supplied to the supported bilayer, a thin actin layer is formed at the membrane surface (Fig. 1, A and B). When we substituted concentrated frog egg extracts for the purified proteins, unusual dense, focal, and long actin structures with a diameter of 0.3 to 1.5 μm rose from the surface of the bilayer (Fig. 1, C to E, fig. S1A, and movies S1 to S4). We term these filopodia-like structures (FLSs).

By means of electron microscopy (EM) using negative stain, we observe bundled actin filaments in the FLSs, which are characteristic of filopodia and distinct from the dendritic networks made by Listeria or ActA beads (Fig. 1, F and G). The parallel alignment of actin filaments is revealed when smaller FLSs spread out two-dimensionally (Fig. 1G). We observed actin bundles of the complete size range seen by light microscopy (fig. S1B). Prefixing the FLSs produces similar actin bundles (fig. S1C).

If FLSs recapitulate filopodia, we would predict that new actin monomers would be added at the membrane-localized tip with dynamics similar to filopodial growth in vivo (*20*, *21*). Time-lapse confocal imaging and *z*-stack reconstructions show that the typical initial rate of FLS growth is 2.5 μm/min, which is within the range of filopodia (Fig. 1H and movies S1 to S4). A pulse-chase experiment starting actin growth with Alexa 647-actin (Invitrogen, Carlsbad, CA) and adding Alexa 488-actin after 20 min shows that actin polymerization occurs at the membrane-localized tip (Fig. 1, I and J, and fig. S1, D to G). Actin monomers are added at 2.8 μm/min (fig. S1H). Growth of the bundles into the membrane is prevented by the underlying glass support; hence, assembly is constrained to occur away from the membrane. With this difference, the assembly of bundled and parallel actin filaments at the membrane recapitulates filopodial formation and growth.

For filopodia in vivo, a distinct collection of proteins was observed by means of EM and termed the tip complex (*5*, *20*). To determine whether such a structure is present in the FLSs, we immunostained for known filopodial components or added fluorescently tagged proteins. Like filopodia, FLSs immunostain for fascin along the length of the structure (Fig. 1K, and antibody specificity is shown in fig. S1I) (*22*). The tip of the FLSs contains proteins that localize to the tips of filopodia—diaphanous-related formins, VASP, profilin, and N-WASP (Fig. 1, L to N and P) (*5*, *8*, *23*–*26*). Cdc42 and toca-1 also localize to the tip (Fig. 1, O and Q). Alexa 568–labeled Arp2/3 complex is enriched at the tip and also decorates the actin shaft (Fig. 1R). In some filopodia, Arp2/3 complex is excluded from the shaft, whereas in others it is present (*5*, *27*).

Tip complex assembly requires negatively charged membranes because no FLSs form on glass or phosphatidylcholine (PC) bilayers alone. A direct comparision of PC/ phosphatidylserine (PS) and PC/PS/phosphatidylinositol 4,5-bisphosphate [$PI(4,5)P_2$] membranes of equivalent net charge shows that there is specificity for $PI(4,5)P_2$, which supports a 2.5-fold higher density of FLSs at steady state (20 min); their initial rate of appearance is also fivefold faster than with just PS (Fig. 2A, blue and orange). Substitution of PS for PI (phosphatidylinositol) leads to a twofold decrease in the rate of appearance, which may reflect the role of PS in binding some F-BAR proteins (Fig. 2A) (*28*). All phosphoinositides (PIPs) nucleate actin spots on the membrane (bis/tris-PIPs are shown in Fig. 2B, and monophosphorylated PIPs are shown in fig. S2A), although few of the actin spots nucleated by monophosphorylated PIPs elongate. Among bisphosphorylated PIPs and phosphatidylinositol 3,4,5-trisphosphate [$PI(3,4,5)P_3$], $PI(4,5)P_2$ gives the highest number and elongation rate (Fig. 2, B and C), which is consistent with filopodia forming on the plasma membrane. One caveat in comparing the different PIPs is that the extracts may convert one form into another.

The tendency of lipid mixtures to segregate into domains suggests two different models for tip assembly and FLS nucleation. In the first, the FLSs would be templated by small domains enriched in $PI(4,5)P_2$. In this model, the size of the tips and the girth of the FLSs should reflect the size of the domains. In the second, tip complexes would self-assemble on the lipid bilayer in relatively homogeneous lipid domains. We found no evidence for preformed domains that template FLS formation because green fluorescent protein (GFP)–phospholipase C–δ pleckstrin homology domain (GFP-PH domain), which has specificity for $PI(4,5)P_2$, binds evenly over large interconnected domains, and there is no enrichment of GFP-PH domains at sites of FLS growth (Fig. 2D and fig. S2, B to D). Furthermore, the kinetics of PH domain binding to the bilayer does not reveal hotspots of $PI(4,5)P_2$ (fig. S2, E and F). Rhodamine–phosphatidylethanolamine (PE), which labels the liquid-disordered phase of membranes (*29*), has the inverse distribution to GFP-PH domain, confirming that lipid is present in regions depleted of the GFP-PH domain. This also indicates that either $PI(4,5)P_2$ partitions differently than rhodamine-PE, or that the GFP-PH domain cannot bind $PI(4,5)P_2$ within these domains (Fig. 2D). Domains of rhodamine-PE enrichment vary in size, with 53% less than 10 μm^2, 38% 10 to 100 μm^2, 7% 100 to 1000 μm^2, and 2% >1000 μm^2. Rhodamine-PE–enriched regions nucleate 95% fewer FLSs than the rhodamine-PE depleted regions (Fig. 2E). DiI, another fluorescent membrane marker that labels the disordered phase, also localizes to areas

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with fewer FLSs (fig. S3A). Fluorescence recovery after photobleaching (FRAP) experiments confirm that the rhodamine-PE–positive regions are fluid (fig. S3, B and C). The irregular boundaries between rhodamine-PE regions and GFP-PH domain regions also suggest the coexistence of the liquid-disordered (rhodamine-PE) and gel phases (GFP-PH domain) (*30*). FRAP of GFP-PH domain confirms the low fluidity of these regions (fig. S3D and E). Thus, FLS formation occurs preferentially but not exclusively in the gel phase. The tendency of FLS not to form from the liquid-

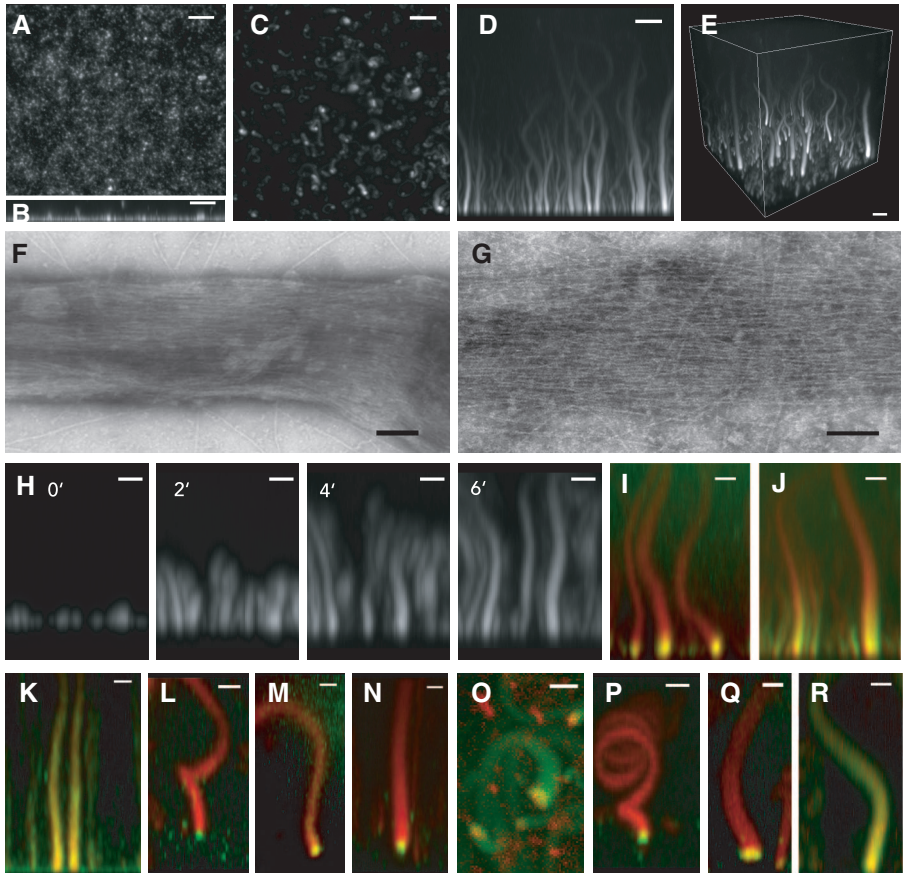

Fig. 1. Reconstitution of filopodia-like structures on supported lipid bilayers containing 45% PC, 45% PI, or 10% PI(4,5)P_2. (**A**) Confocal microscopy of supported bilayers with Cdc42, N-WASP-WIP, toca-1, Arp2/3 complex, and actin generates uniform, short polymerized actin. (**B**) *Z*-stack reconstruction of (A) showing growth of actin in the *z* axis. (**C**) Confocal microscopy of supported lipid bilayers with *Xenopus* egg extracts and Alexa 647-actin (seen along the *x-y* plane) shows growth of focal actin structures from the bilayer. (**D**) *Z*-stack reconstruction looking at the *x-z* plane shows the height of the actin structures. (**E**) Three-dimensional reconstruction. Scale bars, 5 μm. (**F** to **G**) Negative-stain EM of the phalloidin-stabilized actin structures shows that these are made of bundled, unbranched actin filaments. Scale bars, 100 nm. (**H**) Time-lapse sequence of FLS formation seen. Scale bars, 2 μm. (**I** and **J**) Pulse-chase experiments show that actin polymerization occurs at membrane. The reaction is started with Alexa 647-actin (red) and chased by Alexa 488-actin (green). Scale bars, 2 μm. (I) 1 min timepoint. (J) 2 min 40 s timepoint. (**K**) Immunostained FLSs from the side: green, fascin immunostain; red, Alexa 568-phalloidin. (**L**) 60° tilt from the *x-y* plane: green, Drf1 immunostain; red, Alexa 568-phalloidin. (**M**) 60° tilt from the *x-y* plane: green, GFP-VASP; red, Alexa 647-actin. (**N**) 60° tilt from the *x-y* plane: green, profilin immunostain; red, Alexa 568-phalloidin. (**O**) Top view: red, mCherry-Cdc42; green, Alexa 488-actin. (**P**) 60° tilt from the *x-y* plane: green, N-WASP immunostain; red, Alexa 568-phalloidin. (**Q**) 60° tilt from the *x-y* plane: green, GFP-toca-1; red, Alexa 647-actin. (**R**) Side view: red, Alexa 568–Arp2/3 complex; green, Alexa 647-actin. Scale bars, 2 μm.

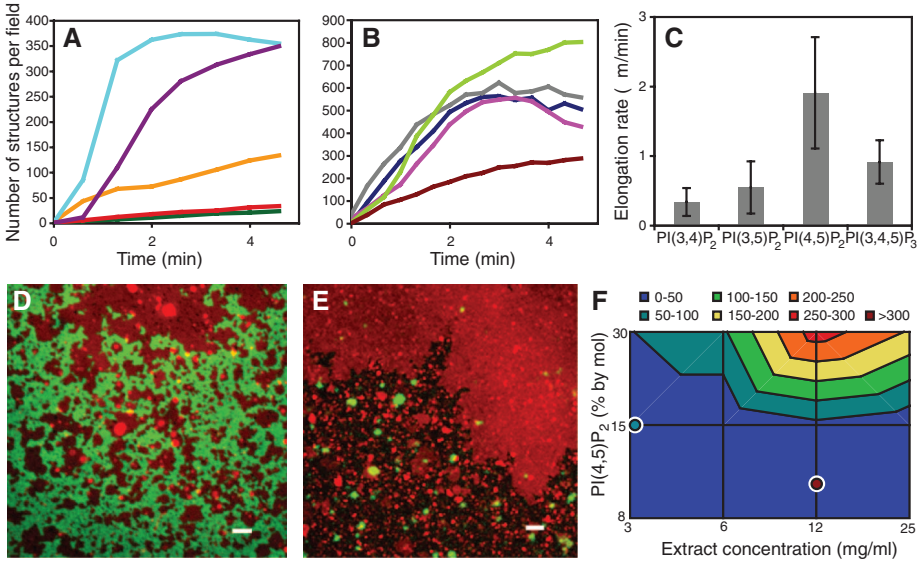

Fig. 2. Membrane requirements for FLS formation. (**A**) Time course of FLS appearance shows that negatively charged lipids are essential for FLS formation and there is specificity for PI(4,5)P_2 and PS. Blue, 60% PC/30% PS/10% PI(4,5)P_2; purple, 60% PC/30% PI/10% PI(4,5)P_2; orange, 40% PC/60% PS; red, 55% PC/45% PS; dark green, 70% PC/30% PS. (**B**) Time course of FLS appearance. All PIPs can nucleate FLSs, but there is preference for PI(4,5)P_2. Compositions are 60% PC/30% PS/10% PIP, where lime indicates PI(4,5)P_2, gray indicates PI(3,4)P_2, purple indicates PI(3,5)P_2, dark blue indicates PI(3,4,5)P_3, and brown indicates PI. Data are the mean of three time courses normalized to the average number of structures from the three experiments from five or more pictures over each supported bilayer. (**C**) Rate of actin addition (using the pulse-chase approach) for the different PIPs shows PI(4,5)P_2 specificity. Error bars are SD; n = 18, 19, 16, 20 FLSs, from left to right. (Four-way analysis of variance, $P < 0.001$). (**D**) Confocal microscopy of supported bilayer surface. GFP-PH domain (green) addition to supported bilayers including rhodamine-PE (red) shows membrane domains. Scale bar, 2 μm. The lipid composition was 45% PC, 45% PI, and 10% PI(4,5)P_2, and similar data was obtained with 60% PC, 30% PS, and 10% PI(4,5)P_2. (**E**) FLSs grow preferentially from rhodamine-PE–depleted (PH domain binding) regions. Alexa 647-actin is in green, and rhodamine-PE is in red. Scale bar, 2 μm. (**F**) Contour plot of the number of FLSs per field of view at steady state (20 min) from fluid membranes in response to PI(4,5)P_2 and extract concentrations. The lipid composition was 45% PC, 45% PI, and 10% PI(4,5)P_2. For comparison, overlaid single points show the number of FLSs formed from the gel phase. Data are plotted logarithmically. Example pictures and control data are in fig. S4.

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disordered phase can be overcome by increasing the mole fraction of PI(4,5)P_2 or by increasing the extract concentration (Fig. 2F and fig. S4), and therefore the gel phase is not an absolute prerequisite for FLS formation.

Thus, the assembly of FLSs does not occur by direct templating at preformed domains in the membrane but instead occurs by a process of self-assembly driven by proteins at a permissive membrane surface. Several mechanisms could contribute to FLS formation: (i) clustering of oligomeric activation proteins [such as Bin–Amphiphysin–Rvs (BAR) domain superfamily proteins] (*31*); (ii) positive feedback on small Arp2/3 complex–catalyzed clusters of polymerized actin through recruitment of more nucleation factors (*32*), such as occurs during symmetry-breaking by N-WASP on lipid-coated glass beads; (iii) lattices generated by cooperative protein-protein interactions between signaling molecules; (iv) cooperative association of proteins with PI(4,5)P_2, as has previously been shown for N-WASP (*33*). Any small local fluctuations in PI(4,5)P_2 could be magnified in such a mechanism.

To investigate the kinetics of the self-assembly process of the FLSs, we added fluorescently labeled filopodial proteins to the extracts and followed their recruitment to sites of FLS formation by using TIRF microscopy (Fig. 3 and fig. S5). The recruitment times are normalized to the recruitment time of labeled actin, with the time differences plotted as a histogram (Fig. 3). The membrane-binding, F-BAR domain protein toca-1 is recruited earliest, at sites that later go on to form FLSs (Fig. 3, A and G). After a variable time, N-WASP is recruited, again before actin (Fig. 3, B and G). The Arp2/3 complex is recruited concomitantly with actin (Fig. 3, C and G). VASP and mDia2 proteins, which are implicated in the formation of long, unbranched actin filaments, are recruited to the tip complex after the first appearance of actin (Fig. 3, D, E, and H). The bundling protein fascin is recruited last (Fig. 3, F and H).

These data suggest that an Arp2/3 complex–driven initiation step nucleates an initial branched actin structure in a small patch, which stimulates the recruitment of filament elongation and bundling factors. To test this mechanism further, we looked at the recruitment of Arp2/3 complex and mDia2 to toca-1 spots in the presence of the actin monomer–sequestering drug latrunculin B. The number of toca-1 spots that recruit Arp2/3 complex are unaffected by latrunculin (Fig. 4A), whereas latrunculin completely blocks toca-1–mDia2 colocalization (Fig. 4A).

To probe the role of the Arp2/3 complex in FLS formation, we added glutathione *S*-transferase cofilin homology and acidic (GST-CA) domain, which inhibits N-WASP activation of the Arp2/3 complex; this reduces the number of nucleation sites and abolishes FLS elongation (Fig. 4B and fig. S6, A and B). Immunodepletion of N-WASP significantly decreases but does not completely inhibit FLS formation and elongation (fig. S6, D and H to I), which is consistent with studies in cultured cells that suggest the involvement of other Arp2/3 complex nucleation–promoting factors (*11*, *12*). Immunodepletion of toca-1 has only a minor effect on elongation (fig. S6, E, H, and I); however, there are more than a dozen candidate BAR domain superfamily proteins that could compensate for loss of toca-1. We conclude that signaling through the Arp2/3 complex plays a vital role in the initiation of FLS formation, although these proteins alone are not sufficient to generate FLSs (Fig. 1, A and B).

The usual product of Arp2/3 complex activation is an array of disorganized or branched actin structures rather than organized parallel actin bundles. The kinetics of protein recruitment to the nascent FLSs suggests that a formin-driven elongation process occurs after the formation of the first actin nucleus. To test whether the elongation phase is dependent on the Arp2/3 complex, we started the reaction with Alexa 647-actin and Alexa 568–Arp2/3 complex and after 20 min added GST-CA to block further Arp2/3 complex function and Alexa 488-actin to record any further actin polymerization (Fig. 4, C to H). We found that new actin monomers are still added at the FLS tip after Arp2/3 complex inhibition (Fig. 4, C to F). In the presence of GST-CA, there is no further incorporation of Arp2/3 complex into the FLS. The region of newly assembled actin in the shaft lacks Arp2/3 complexes (Fig. 4, E and F, and fig. S7A). After ~5 min, addition of new actin to the FLS slows, indicating a requirement for Arp2/3 complex to maintain FLS growth over the long term (Fig. 4G). At high concentrations of GST-CA, there is a noticeable lag in the incorporation of new actin monomers (Fig. 4G), probably because the occupancy of GST-CA on N-WASP–binding sites of the Arp2/3 complex stimulates a reorganization of the tip complex. Even at high doses of GST-CA, an Arp2/3 complex–independent component of elongation is maintained (Fig. 4H).

Diaphanous-related formins are the obvious engine for filopodial growth in the absence of the Arp2/3 complex because formins are thought to drive filopodial elongation in different cell types. Because there are many formin proteins, we used a dominant-negative approach known to inhibit filopodia formation (*34*, *35*). The leucine-rich region (LRR) of diaphanous-interacting protein (DIP) binds and inhibits Drf1 and Drf3 (*35*). When GST-DIP-LRR is added to extracts, FLS formation

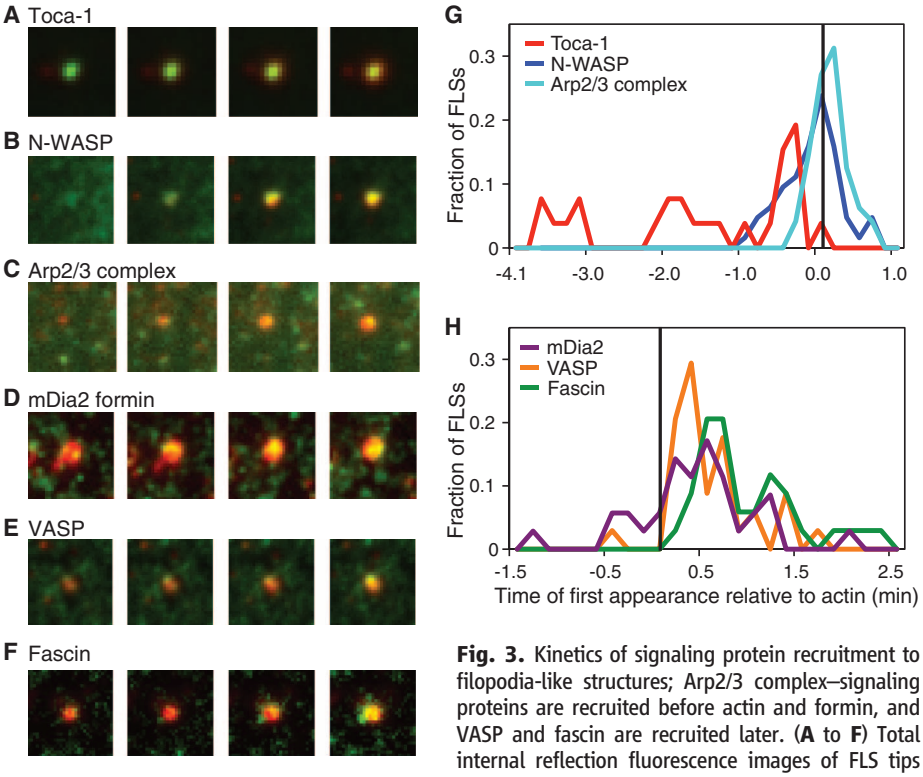

Fig. 3. Kinetics of signaling protein recruitment to filopodia-like structures; Arp2/3 complex–signaling proteins are recruited before actin and formin, and VASP and fascin are recruited later. (**A** to **F**) Total internal reflection fluorescence images of FLS tips with fluorescently labeled proteins (GFP-toca-1, GFP-N-WASP, Alexa 568–Arp2/3 complex, GFP-mDia2, GFP-VASP, and GFP-fascin) are in green, and Alexa 647-actin is in red. Time intervals of 20 s are shown at the time of first recruitment of the signaling protein or actin. 5 nM–labeled proteins were added to the extracts. (**G**) Histogram showing the relative time of first recruitment of Arp2/3 complex (n = 48 FLSs), toca-1 (n = 26 FLSs), and N-WASP (n = 34 FLSs) compared with the first appearance of actin. (**H**) Histogram showing the relative time of first recruitment for filopodia elongation and bundling proteins, VASP (n = 34 FLSs), mDia2 (n = 35 FLSs), and fascin (n = 34 FLSs) compared with actin. Using the KS-test, P = 0.000 for toca-1-N-WASP, N-WASP-Arp2/3 complex, and Arp2/3 complex-VASP; P = 0.005 for Arp2/3 complex-mDia2; P = 0.003 for mDia2-fascin; and P = 0.004 for VASP-fascin and no significant difference for mDia2-VASP. The lipid composition was 60% PC, 30% PS, and 10% PI(4,5)P_2.

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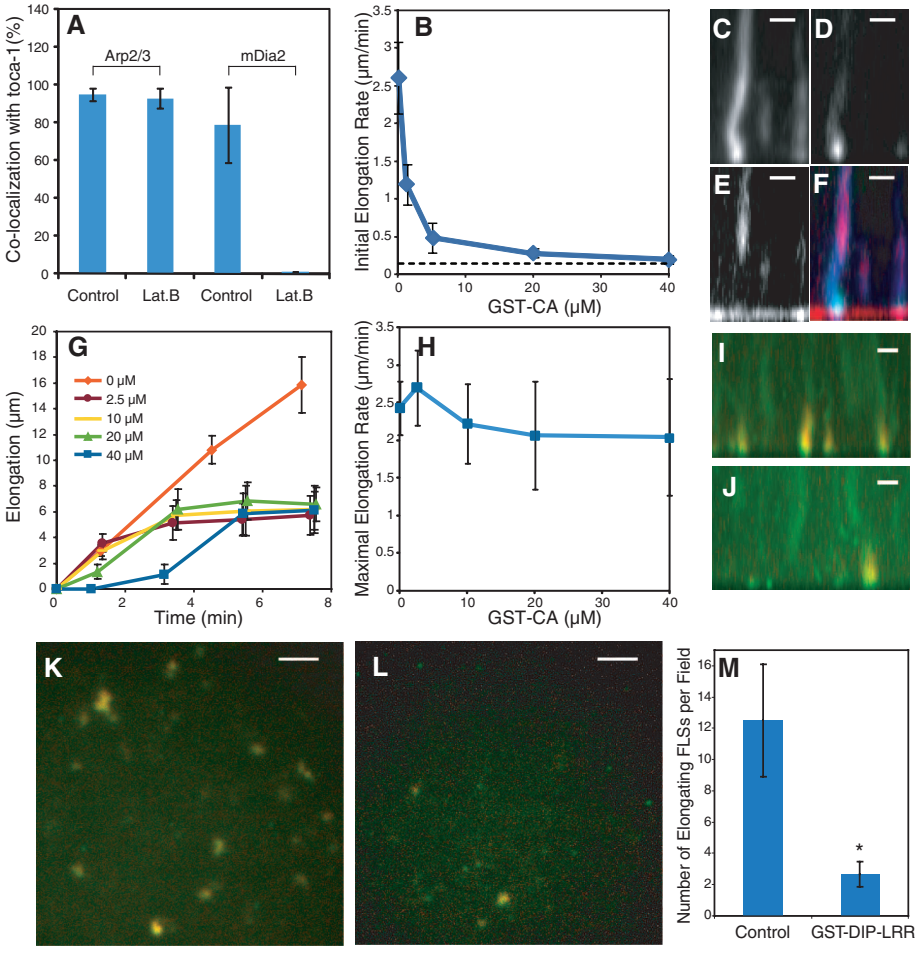

Fig. 4. Initiation and elongation of FLSs occur by means of separable molecular mechanisms. (**A**) Latrunculin B does not affect the co-localization of Arp2/3 complex with toca-1 but completely inhibits mDia2 recruitment to toca-1 sites (n = 4 independent experiments). (**B**) Dose-response of FLS initial elongation rate with GST-CA preincubated in the extract before addition to the supported bilayer (n = 20 FLSs). The dotted line indicates the minimum elongation rate (0.1 μm/min) attributable to the axial resolution limit of confocal microscope (~0.7 μm). (**C** to **F**) Pulse-chase experiment starting with Alexa-647 actin and Alexa 568-labeled Arp2/3 complex in the extract, with later addition of 40 μM GST-CA and Alexa-488 actin. Shown are Alexa 647-actin [(C), blue]; Alexa 488-actin [(D), green]; Alexa-568-Arp2/3 complex [(E), red]; and a three-color overlay (F). Addition of new actin monomers continues in the absence of the Arp2/3 complex recruitment into the FLS. Scale bars, 2 μm. (**G**) The time course of FLS elongation (measured by the second color of actin) at increasing GST-CA concentrations (n = 20 FLSs). (**H**) Dependence of rate of FLS elongation on the concentration of GST-CA. Maximal FLS elongation rate is unchanged by addition of GST-CA. (**I** to **M**) Similar pulse-chase experiment explained in (C) to (H), with the additional use of GST-LRR to inhibit formin activity. [(I) and (K)] Control addition of GST-CA plus the second color of actin: Alexa-647 (red) was first, and Alexa-488 (green) was second. (I) Side view. (K) Actin on the bilayer. (J and L) Inclusion of 5 μM GST-LRR in the extract, then addition of GST-CA and Alexa-488 actin. GST-LRR leads to the detachment of the FLSs so that fewer punctae are present at the membrane surface. (J) Side view. (L) Actin on bilayer. Scale bars, 2 μm [(I) and (J)] and 5 μm [(K) and (L)]. (M) Quantification of GST-DIP-LRR addition (n = 6 fields of view). *P < 0.001. All error bars are SD. The lipid composition was 45% PC, 45% PI, and 10% PI(4,5)P_2.

still occurs with no reduction in elongation rate or the number of structures. However, when Arp2/3 complex function is inhibited by GST-CA in the presence of GST-DIP-LRR, the number of structures that incorporates new actin monomers is significantly reduced (Fig. 4, I to M). This is accompanied by the detachment of many FLSs from the lipid bilayer, suggesting that the tip complex undergoes conformational changes and that continuing reorganization of the tip complex cannot occur in the presence of GST-LRR (Fig. 4M). Furthermore, because diaphanous-related formins are activated by RhoA we also tested dominant-negative RhoA, GST-RhoA-N19. This produced similar results to GST-DIP-LRR (fig. S7, B to F). Thus, there are important functions contributed by both the Arp2/3 complex and formins. In the presence of capping activities, the Arp2/3 complex may be required for generating new actin nuclei (*7*, *36*).

Currently, there are two principal models for filopodial assembly: convergent elongation (*5*) and de novo nucleation (*37*). In the former, Arp2/3 complex–driven actin filaments continually coalesce into parallel arrays through the continuous action of bundling proteins, such as fascin. In the latter, filopodia are formed through the establishment of a tip complex of formins, which nucleates long actin filaments that are then bundled. In the model we propose (fig. S8), signaling by a negatively charged membrane leads first to the recruitment and clustering of BAR domain superfamily proteins and N-WASP or other nucleation promoting factors at the membrane, leading to subsequent recruitment of the Arp2/3 complex and the formation of a small patch of short actin filaments. This early clustering step represents the key difference from the convergent elongation model because symmetry-breaking occurs through the focal recruitment of activators of the Arp2/3 complex rather than by a coalescence of preexisting actin-barbed ends. In the proposed clustering-outgrowth model, local assembly of actin initiated by the Arp2/3 complex is converted into a filopodial tip complex by the recruitment of formins and VASP. This recruitment enables linear outgrowth of the filopodium, with short actin filaments elongated by formins and/or VASP and bundled by fascin (*15*, *16*). Actin filaments generated by the Arp2/3 complex appear to be continually required to feed the elongation process, although other actin nucleators could fulfill a similar role. The observation of short actin filaments at the tips of filopodia in *Dictyostelium* by means of electron tomography is consistent with this model (*38*). The clustering of actin assembly proteins and outgrowth by elongation factors may be served by different components in different circumstances. In this view, we should expect that although the overall mechanism would be conserved, there could be flexibility in filopodial composition (*39*).

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Supporting Online Material

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Movies S1 to S4

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Aryl Hydrocarbon Receptor Antagonists Promote the Expansion of Human Hematopoietic Stem Cells

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Although practiced clinically for more than 40 years, the use of hematopoietic stem cell (HSC) transplants remains limited by the ability to expand these cells ex vivo. An unbiased screen with primary human HSCs identified a purine derivative, StemRegenin 1 (SR1), that promotes the ex vivo expansion of CD34$^+$ cells. Culture of HSCs with SR1 led to a 50-fold increase in cells expressing CD34 and a 17-fold increase in cells that retain the ability to engraft immunodeficient mice. Mechanistic studies show that SR1 acts by antagonizing the aryl hydrocarbon receptor (AHR). The identification of SR1 and AHR modulation as a means to induce ex vivo HSC expansion should facilitate the clinical use of HSC therapy.

The identification of pharmacological agents that control adult or embryonic stem cell fate has the potential to facilitate the application of stem cell therapies to a host of diseases (*1*). Among the best-characterized adult stem cells are hematopoietic stem cells (HSCs) (*2*). Although HSCs are widely used, their full clinical potential has yet to be realized due to lack of defined culture conditions for their expansion (*3*). This is especially true of allogeneic HSC transplants in which only 50% of candidates can find a human leukocyte antigen (HLA)–matched adult donor (*4*). The use of cord blood (CB)–derived HSCs is an alternative, because the large number of banked CB units greatly facilitates finding an HLA-matched graft (*5*). However, the low number of HSCs in these units has largely restricted the widespread application of CB HSCs to the pediatric setting (*6*). To overcome this limitation, clinicians are transplanting CB units from two donors with encouraging preliminary results (*7*), which suggests that even a twofold increase in HSC number would substantially affect HSC transplantation. Thus, identification of molecules that expand HSCs during ex vivo culture has remained an important goal of the field.

Culture conditions optimized for HSC expansion (serum-free media supplemented with thrombopoietin, stem cell factor, flt3 ligand, and interleukin-6; referred to as "cytokines" hereafter) (*8*) result in robust proliferation accompanied by differentiation, leading to loss of HSC activity. This differentiation can be followed by the loss of the cell-surface proteins CD34 and CD133, which are expressed on HSCs and progenitor cells (Fig. 1A) (*9*). Thus, to identify molecules that promote HSC expansion, we developed an assay that uses primary human CD34$^+$ cells from the blood of mobilized donors (mPB) (*10*) and evaluated CD34 and CD133 expression by confocal microscopy after a 5-day culture (Fig. 1A) (*11*). Using this assay, we screened a library of 100,000 heterocycles (*12*) and identified a purine derivative [StemRegenin 1 (SR1)] (Fig. 1B) that increases the number of CD34$^+$ cells after 5 to 7 days with a half-maximal effective concentration (EC_{50}) of ~120 nM (Fig. 1A, fig. S1, and table S1). We analyzed a structure-activity–relationship study of a 2,6,9-substituted purine library based on SR1. Representative analogs and their EC_{50} values are provided in the supporting online material (figs. S2 to S4) (*11*).

Culture of mPB CD34$^+$ cells with cytokines plus SR1 (hereafter referred to collectively as SR1, unless noted as SR1 alone) for 7 days increased the number of CD34$^+$, CD133$^+$, and CD90$^+$ hematopoietic stem and progenitor cell populations 2.6-, 2.3-, and 10-fold, respectively (Fig. 1C, fig. S5A, and table S1), compared with control cells [defined as cultures with cytokines plus vehicle (dimethylsulfoxide, ≤0.01%)]. Continued culture with SR1 for 3 weeks led to an 11-fold increase in total nucleated cells (TNCs), a 73-fold increase in CD34$^+$ cells compared with control cultures, and a 1118-fold increase in CD34$^+$ cells relative to input cells (fig. S5B and table S2). Removal of SR1 led to rapid differentiation, indicating that the effect of SR1 is reversible (fig. S6). SR1 in the absence of cytokines did not induce proliferation, and at concentrations above 1 μM, SR1 treatment is antiproliferative (fig. S7). Culture with SR1 had no effect on murine HSCs but did expand CD34$^+$ cells from bone marrow of humans, monkeys (cynomolgus and rhesus), and dogs (fig. S7). SR1 also maintains CB precursors at a less differentiated stage (Fig. 1D). Culture of human CB CD34$^+$ cells for 5 weeks with SR1 resulted in a 17,100-fold expansion compared with input cells, a 10-fold increase in TNCs, and a 47-fold increase in CD34$^+$ cells and CD34$^+$ subpopulations (e.g., CD34$^+$CD45RA$^-$ enriched in HSCs and multilineage progenitor cells) compared with control cells (Fig. 1, D and E, and table S3A).

We next used the cell-division–monitoring dye carboxyfluorescein succinimidyl ester to determine if the increase in the number of CD34$^+$ cells results from symmetric division. After 7 days, the cells had undergone six to nine divisions, regardless of the presence of SR1, indicating that SR1 does not affect the division rate (fig. S8, A and B). SR1-treated cells retained high levels of CD34 expression (66 to 76%), whereas cells cultured with cytokines alone lost CD34 expression (14 to

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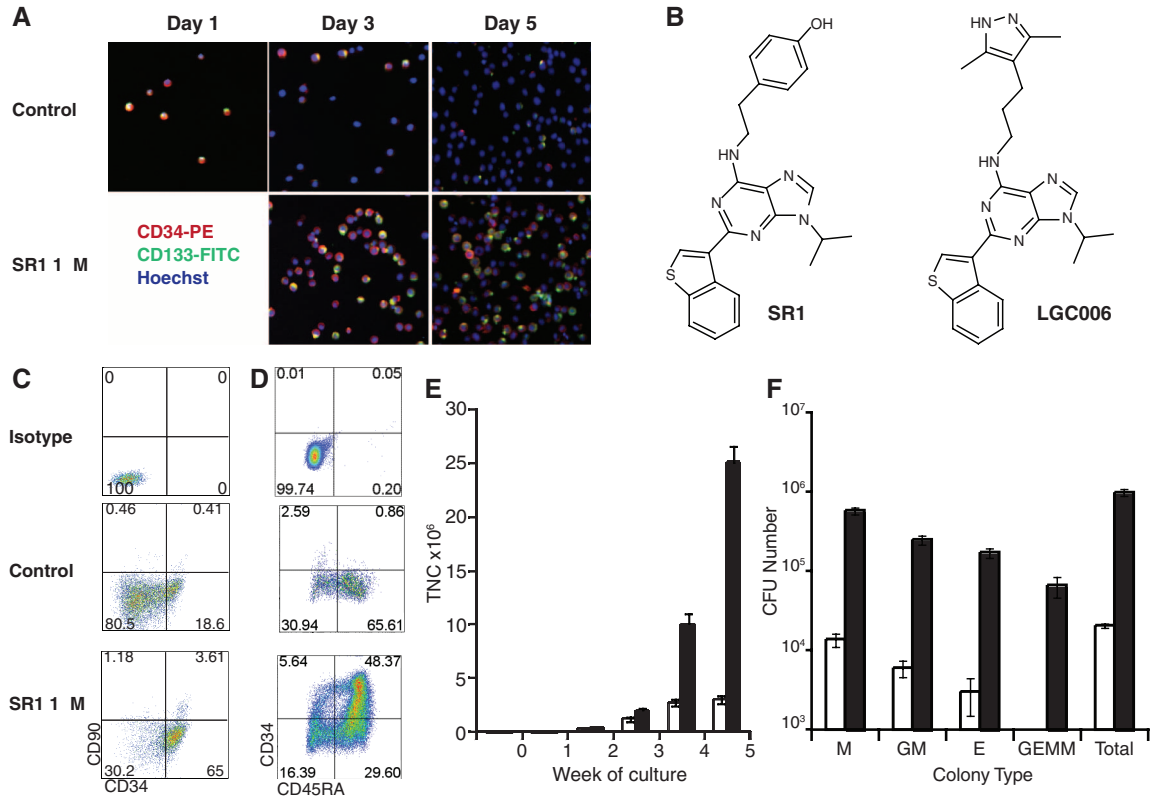

Fig. 1. SR1 maintains an HSC phenotype and increases CFU content. (**A**) Expression of CD34 and CD133 in cultured mPB CD34$^+$ cells. (**B**) Structures of SR1 and LGC006. (**C**) Phenotype of CD34$^+$ mPB at 7 days or (**D**) CB at 35 days. (**E**) Weekly TNC counts from control (white bars) or SR1 (1 μM, black bars) cultures of 1000 CB CD34$^+$ cells. Error bars indicate standard deviations of triplicate cultures. (**F**) Total CFU content of control (white bars) or SR1 (1 μM, black bars) cultures of 1000 CB CD34$^+$ cells at 5 weeks. M, myeloid; GM, granulocyte/monocyte; E, erythroid; GEMM, granulocyte, erythroid, monocyte, and megakaryocyte colonies.

31%) (fig. S8C). Thus, SR1 promotes the retention of CD34 expression after ex vivo culture.

SR1 also expands the number of colony-forming units (CFUs). Culture of 1000 CB CD34$^+$ cells for 5 weeks with SR1 resulted in the production of 169 × 10^4 CFUs, a 65-fold increase compared with control cells and a >9500-fold increase over input cells (Fig. 1F and table S3B). This includes increases in the number of single-lineage myeloid (M, 55-fold), erythroid (E, 129-fold), and bipotential granulocyte/monocyte (GM, 55-fold) colonies. We detected multilineage granulocyte, erythroid, monocyte, and megakaryocyte (GEMM) colonies only in the SR1-expanded cells, suggesting that SR1 promotes the expansion of early multipotent progenitors.

Next, we asked whether SR1-expanded CB CD34$^+$ cells engraft NOD.Cg-Prkdcscid Il2rgtm1Wjl/SzJ (NSG) mice (*13*). Human cells capable of hematopoietic reconstitution in these mice are termed NOD-SCID repopulating cells (SRCs) and represent candidate human HSCs. We cultured 250,000 CB CD34$^+$ cells for 3 weeks with control conditions (1080-fold expansion) or SR1 (2024-fold expansion) (table S4). We transplanted 300 to 30,000 uncultured CB CD34$^+$ cells (or a fraction of the final culture equivalent to 300 to 10,000 starting cells) into NSG mice (see fig. S9 for cell-surface phenotype). CB CD34$^+$ cells cultured with SR1 generated significant increases in human engraftment in the peripheral blood at 1 week, compared with mice transplanted with 10,000 uncultured cells (sixfold, $p < 0.05$) or the progeny of 10,000 control cells (24-fold, $p <$

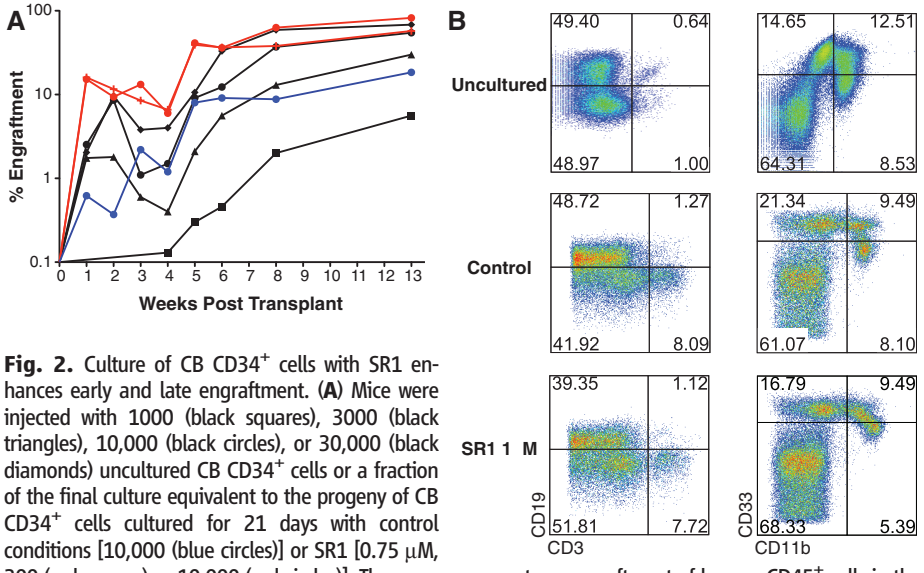

Fig. 2. Culture of CB CD34$^+$ cells with SR1 enhances early and late engraftment. (**A**) Mice were injected with 1000 (black squares), 3000 (black triangles), 10,000 (black circles), or 30,000 (black diamonds) uncultured CB CD34$^+$ cells or a fraction of the final culture equivalent to the progeny of CB CD34$^+$ cells cultured for 21 days with control conditions [10,000 (blue circles)] or SR1 [0.75 μM, 300 (red crosses) or 10,000 (red circles)]. The average percentage engraftment of human CD45$^+$ cells in the blood (weeks 1 to 8) and BM (week 13) is shown. (**B**) Representative flow cytometry plots showing myeloid (CD11b and CD33) and lymphoid (CD19 and CD3) engraftment in the bone marrow.

0.05) (Fig. 2A). The progeny of 300 CB CD34$^+$ cells expanded with SR1 generated the same level of sustained engraftment as 10,000 uncultured CB CD34$^+$ cells and a fourfold increase in human engraftment, as compared with control cells at 8 weeks in the peripheral blood and 13 weeks in the bone marrow (BM) (Fig. 2A and fig. S10, A and B). These results demonstrate that SR1 promotes expansion of CB CD34$^+$ cells that contribute to both early and sustained engraftment. The distribution of human B, T, and myeloid cells in the BM, spleen, and thymus was similar for all groups (Fig. 2B, fig. S11, A to C, and fig. S12). These data demonstrate that CB CD34$^+$ cells expanded with SR1 retain multilineage potential.

To calculate the SRC frequency of SR1-expanded cells, we performed a second engraftment experiment. We transplanted a fraction of the final culture (equivalent to between 30 and 3000 starting CB CD34$^+$ cells expanded for 21

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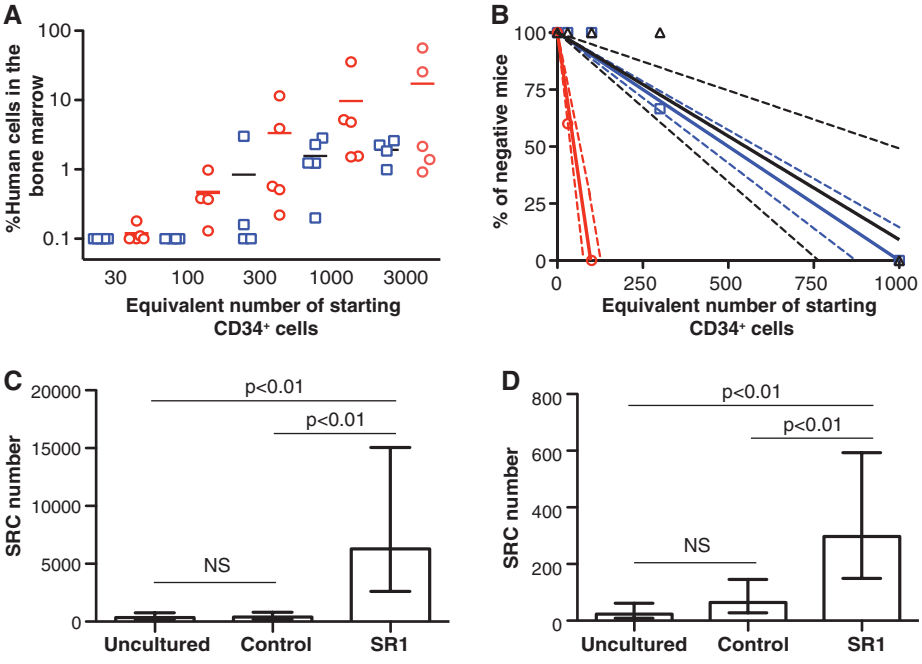

Fig. 3. Culture of CB-derived CD34$^+$ cells with SR1 increases SRC numbers. (**A**) Mice were injected with a fraction of the final culture equivalent to the indicated number of starting CB CD34$^+$ cells after culture for 21 days with control conditions (open blue squares) or SR1 (0.75 μM, open red circles). The percentage of human CD45$^+$ cells in the BM at 16 weeks is shown. Horizontal lines indicate the average of each group. (**B**) Linear-regression analysis of data from Figs. 2A and 3A. Solid lines indicate the best-fit linear regression model for each data set; dotted lines represent the 90% confidence intervals. Shapes (open red circles, open blue squares, open black triangles) represent the percentage of negative animals for each dose of cells (**C**) and secondary (**D**) SRCs before and after culture of 2.5 × 10^5 CB CD34$^+$ cells (calculated using Poisson statistics applied to the data in table S5A). Error bars indicate 95% confidence intervals. NS, not significant.

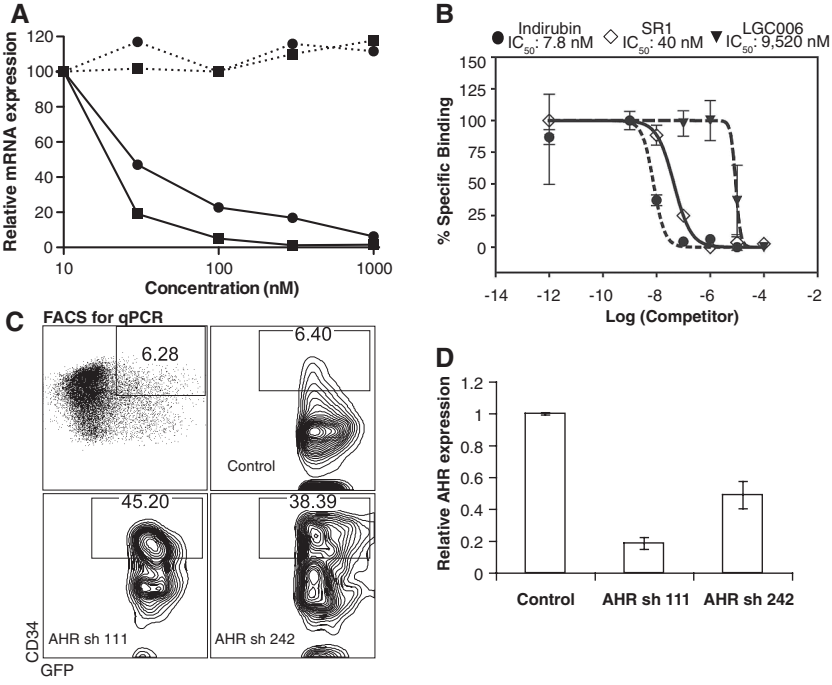

Fig. 4. SR1-induced CD34$^+$ cell expansion acts by binding and antagonizing AhR. (**A**) Percent decrease in CYP1B1 (black squares) and AHRR (black circles) mRNA from mPB CD34$^+$ cells treated with SR1 (solid lines) or LGC006 (dashed lines) for 24 hours. (**B**) Quantification of AhR binding shown in fig. S16. (**C**) Phenotype of GFP$^+$ cells 8 days after transduction with lentivirus expressing shRNAs targeting AhR. FACS, fluorescence-activated cell sorting; qPCR, quantitative polymerase chain reaction. (**D**) Relative AhR mRNA expression in sorted CD34$^+$GFP$^+$ cells [boxes in (C)]. Error bars indicate the standard deviation of replicate determinations.

days with control conditions or SR1) into NSG mice (Fig. 3A). Poisson statistics revealed a SRC frequency of 1 out of 703 (1/703) for uncultured cells, 1/597 per starting cell after cytokine expansion, and 1/40 per starting cell after expansion with SR1 (Fig. 3B). This represents a total SRC content of 356 in the 2.5 × 10^5 CB CD34$^+$ cells used to initiate the cultures, 403 SRCs in control cultures, and 6283 SRCs after culture with SR1 (Fig. 3C and table S5). The increase in NSG engraftment after culture with SR1 was reproducible over seven independent experiments (table S6). Calculation of the SRC numbers based on the number of cells injected after culture revealed that control cultures had a 1000-fold reduction in the SRC frequency, but not total SRC content relative to fresh cells, reflecting that the majority of cells in these cultures are progenitor cells that have lost the ability to engraft NSG mice. Inclusion of SR1 diminished this effect and resulted in an eightfold increase in the SRC frequency relative to control cultures. This result, together with the twofold increase in total cell number, accounts for the 17-fold increase in SRC content.

To determine if SR1-expanded cells are capable of long-term engraftment, we injected bone marrow from primary mice into secondary NSG mice, and mice containing >0.1% human CD45$^+$ cells in the BM 15 weeks after transplant were scored positive (see fig. S13 for examples of positive and negative animals). Poisson statistics revealed a secondary SRC frequency of 1/10,723 for uncultured cells, 1/3749 for control cultures, and 1/841 for cells cultured with SR1 (Fig. 3D and table S5). Thus, the secondary SRC content per 2.5 × 10^5 CD34$^+$ starting cells is 23 for uncultured cells, 64 for control cultured cells, and 297 for cells cultured with SR1 (a 12-fold increase in the number of secondary SRCs as compared to input) (Fig. 3D and table S5). The primary and secondary SRC content of control cultures was unchanged, consistent with the lack of clinical benefit following transplantation of cells expanded under similar conditions (*14*). These data demonstrate that culture with SR1 promotes the expansion of cells that retain multilineage long-term engraftment.

To identify the mechanism by which SR1 increases engraftment potential of CB CD34$^+$ cells, we profiled SR1 across 61 kinases and found no inhibitory activity (table S7). Transcriptional profiling of SR1 and LGC006, a less potent SR1 analog (EC_{50} ~ 3 μM) (Fig. 1B), revealed two genes that were significantly repressed by SR1 treatment and not affected by LGC006-cytochrome P450 1B1 (*CYP1B1*) and the aryl hydrocarbon receptor repressor (*AHRR*). Both are transcriptionally regulated by the aryl hydrocarbon receptor (AHR) (Fig. 4A and table S8), suggesting that SR1 could be acting as an antagonist of AhR signaling. To test this hypothesis, we determined the ability of SR1 to block induction of CYP1B1 mRNA by the AHR agonist dioxin (TCDD) in mPB CD34$^+$ cells. SR1 dose-dependently inhibited the TCDD-induced increase in CYP1B1 mRNA, indicating that SR1 can antagonize AHR signaling in CD34$^+$

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cells (fig. S14A). SR1 also abolished TCDD-induced, AHR-dependent transcription in cells expressing a human AhR–dependent luciferase reporter gene (hDRE-luc) (*15*), demonstrating that SR1 is a potent AHR antagonist [half-maximal inhibitory concentration (IC_{50}) = 127 nM] (fig. S14B). SR1 only weakly inhibited TCDD-induced transcription in murine cells and had no activity on rat cells, suggesting that SR1 preferentially inhibits human AHR. This observation correlates with the lack of activity of SR1 on murine HSCs and may explain the species selectivity of SR1 (table S9). We also tested two other AHR antagonists [alpha-naphthoflavone (*16*) and CH-223191 (*17*)], and both led to dose-dependent increases in the number of $CD34^+$ cells (fig. S15).

To elucidate whether the antagonizing effects of SR1 on AHR signaling are mediated by direct interaction with this nuclear receptor, we used a competitive binding assay between SR1 and AHR photoaffinity ligand (PAL) in liver cytosol isolated from h*AHR* transgenic mice (*18*). SR1 and the high-affinity AHR agonist (indirubin) both inhibited PAL binding (IC_{50} = 40 and 8 nM, respectively), whereas the inactive analog LGC006 was much less effective (IC_{50} = 9520 nM) (Fig. 4B and fig. S16). These results support the conclusion that SR1-induced $CD34^+$ cell expansion is mediated through direct binding and inhibition of the AHR.

To show a direct role for AHR in SR1-induced $CD34^+$ cell expansion, we infected CB $CD34^+$ cells with lentiviruses that express green fluorescent protein (GFP) and short hairpin–mediated RNAs (shRNAs) targeting AHR. In the $CD34^+GFP^+$ cells, both shRNAs led to decreases in AHR mRNA and protein expression (Fig. 4, C and D, and fig. S17A). shRNA knockdown of AHR led to sustained CD34 expression during culture, similar to that observed with SR1 (Fig. 4C and fig. S17, B and C). To determine if SR1-induced $CD34^+$ cell expansion requires inhibition of AHR activity, a constitutively active version of AHR lacking the ligand-binding domain (CA-AHR) was expressed (*19*). SR1 failed to inhibit hDRE-luc activity of HepG2 cells expressing CA-AHR, but it did inhibit dioxon-induced AhR activity in wild-type (WT) HepG2 cells and cells overexpressing WT AHR (fig. S18A). Similarly, SR1 had no effect on CB $CD34^+$ expressing CA-AHR (fig. S18B). Collectively, these data provide strong support that SR1 increases the number of CB-$CD34^+$ cells by direct binding and inhibition of the AHR.

Our data and that of others show that AHR is expressed in HSCs (*20*). In addition to its role as a ligand-activated transcription factor responsible for the induction of drug-metabolizing enzymes, AHR has been implicated in pathways regulating hematopoiesis, including HES-1–, c-MYC–, C/EBP-, PU.1-, β-catenin–, CXCR4-, and STAT5-dependent processes (*21*). Moreover, TCDD treatment of donor mice leads to a decrease in the reconstitution activity of $Lin^-cKit^+Sca\text{-}1^+$ cells (*22*, *23*). These findings strongly implicate AHR in HSC biology; however, future studies are required to define the molecular mechanisms involved in these processes.

One major question is whether the increase in SRC numbers elicited by SR1 reflects expansion of HSCs or indirect mechanisms, such as expansion of facilitator cells. The current data—which show that SR1 increases phenotypic HSC numbers, SR1 and AHR knockdown maintain CD34 expression, and SR1 expands multilineage CFUs—are consistent with AHR antagonists acting to promote SRC numbers by preventing differentiation of HSCs. However, the lack of a suitable in vivo transplantation assay capable of reading out the activity of single human HSCs makes it impossible to exclude alternative mechanisms. Better markers for human HSCs, bioassays capable of reading out single human HSCs, and clinical studies are required to address this important question.

Our results complement previously reported efforts to either enhance the expansion of HSCs [with Notch ligands, angiopoietins, copper chelators, glycogen synthase kinase 3β inhibitors, or the expression of *HOX* genes (*3*)] or increase HSC homing [with prostaglandin E2 (*24*), inhibition of CD26 (*10*), or fucosylation (*25*)] to improve HSC transplant outcomes. To this end, it will be important to explore the clinical potential of SR1, either by itself or in synergy with other agents, to improve outcomes and expand applications of autologous and allogeneic HSC transplantation.

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Supporting Online Material

www.sciencemag.org/cgi/content/full/science.1191536/DC1
Materials and Methods
Figs. S1 to S18
Tables S1 to S9

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Human SIRT6 Promotes DNA End Resection Through CtIP Deacetylation

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SIRT6 belongs to the sirtuin family of protein lysine deacetylases, which regulate aging and genome stability. We found that human SIRT6 has a role in promoting DNA end resection, a crucial step in DNA double-strand break (DSB) repair by homologous recombination. SIRT6 depletion impaired the accumulation of replication protein A and single-stranded DNA at DNA damage sites, reduced rates of homologous recombination, and sensitized cells to DSB-inducing agents. We identified the DSB resection protein CtIP [C-terminal binding protein (CtBP) interacting protein] as a SIRT6 interaction partner and showed that SIRT6-dependent CtIP deacetylation promotes resection. A nonacetylatable CtIP mutant alleviated the effect of SIRT6 depletion on resection, thus identifying CtIP as a key substrate by which SIRT6 facilitates DSB processing and homologous recombination. These findings further clarify how SIRT6 promotes genome stability.

Double-strand breaks (DSBs) are highly cytotoxic DNA lesions that can be repaired by homologous recombination, a highly coordinated process restricted to the S and G_2 phases of the cell cycle (*1*, *2*). Homologous recombination is instigated by DSB end resection (*3*, *4*), which generates single-stranded DNA (ssDNA) through the combined actions of proteins that

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include CtIP [C-terminal binding protein (CtBP) interacting protein] (*5*, *6*) and the tumor suppressor protein BRCA1 (*7*). This ssDNA is bound by replication protein A (RPA), leading to the formation of a ssDNA-RAD51 nucleoprotein filament that mediates homologous recombination. Regulation of these events is critical for cell survival under both normal and DNA-damaging conditions; inherited or acquired deficiencies in DNA repair cause developmental defects, infertility, immune deficiency, neurodegenerative disease, heightened cancer predisposition, and aspects of premature aging (*8*).

We examined the effects of two protein lysine deacetylase (KDAC) inhibitors (*9*, *10*) on DNA damage response signaling triggered by camptothecin (CPT), a topoisomerase I inhibitor that induces replication-dependent DSBs that are repaired by homologous recombination. Sodium butyrate (NaB) inhibits class I and class II KDACs (*10*), whereas nicotinamide inhibits the NAD^+ (nicotinamide adenine dinucleotide)–dependent sirtuin (class III) family of KDACs (SIRT1 to SIRT7) (*9*). We initially confirmed the efficacy of KDAC inhibitors in human U2OS cells (fig. S1, A and B) and found that such treatments did not appreciably affect cell cycle profiles (fig. S1C). Although NaB did not affect CPT-induced DNA damage response signaling (Fig. 1A), nicotinamide specifically impaired RPA phosphorylation on Ser^4 and Ser^8 (Fig. 1A), a marker for resected CPT-induced DSBs (*5*, *11*). Consistent with this finding, nicotinamide-treated cells were impaired in forming RPA and ssDNA foci at CPT-induced lesions (Fig. 1B). Similar defects in RPA phosphorylation and formation of RPA foci were observed in human HeLa cells pretreated with nicotinamide (fig. S2, A and B). Nicotinamide not only impaired resection but also inhibited the CPT-induced formation of RAD51 foci (fig. S3, A and B), decreased homologous recombination (Fig. 1C) (*12*), and caused CPT hypersensitivity (Fig. 1D). Similarly, nicotinamide impaired resection-dependent signaling after treatment of cells with the topoisomerase II inhibitor etoposide (Fig. 1E). The failure of nicotinamide to inhibit phosphorylation of the checkpoint kinase CHK2 or the histone H2AX is consistent with these marks being independent of resection. However, upon nicotinamide treatment we noted essentially normal CHK1 phosphorylation (a mark associated with resected CPT-induced DSBs; fig. S3C), which suggests that CHK1 activation has a low threshold for resection.

Thus, DSB resection and homologous recombination are likely promoted by a KDAC of the sirtuin family. Of the seven human sirtuins, only SIRT1, SIRT6, and SIRT7 are nuclear (*13*), with SIRT1 (*14*, *15*) and SIRT6 (*16*–*18*) having been implicated in maintaining genome integrity. We found that small interfering RNA (siRNA)–mediated SIRT1 depletion caused no discernible defects in DNA damage response signaling (Fig. 2A). In contrast, although SIRT6 depletion did

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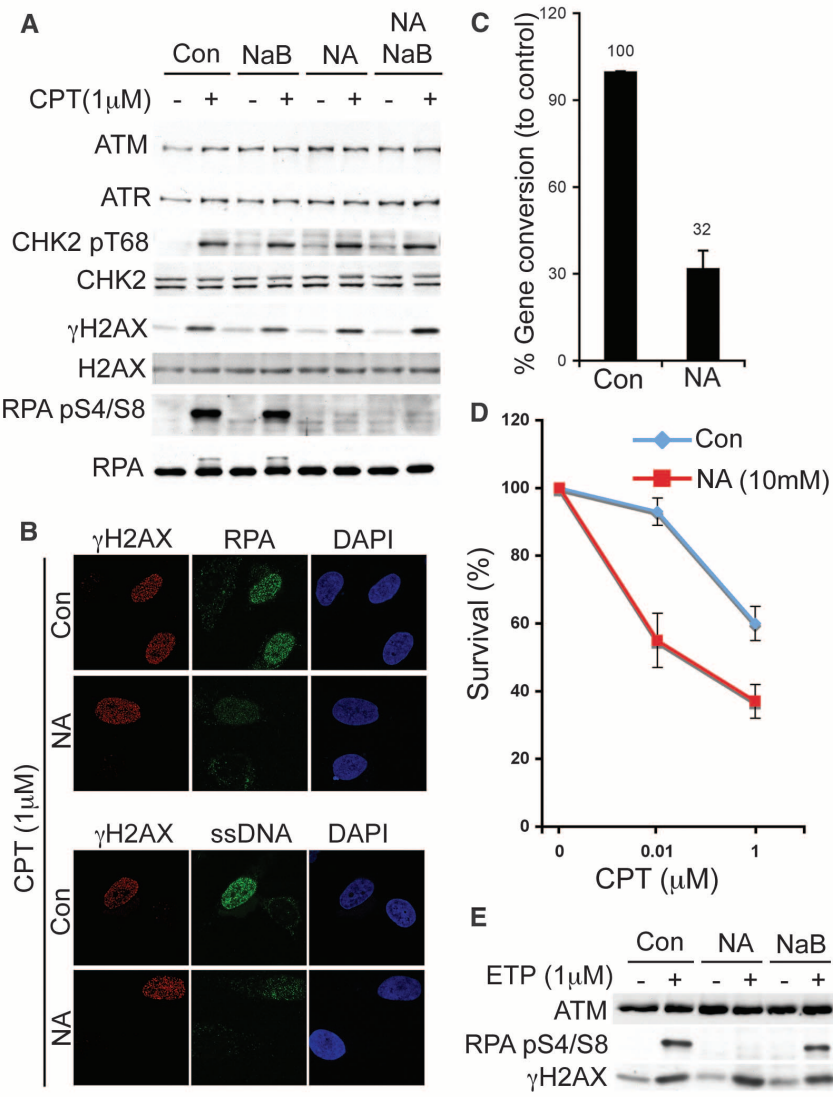

Fig. 1. Nicotinamide treatment impairs resection and homologous recombination. (**A**) U2OS cells were untreated (Con) or pretreated with nicotinamide (NA) and/or NaB, then exposed to CPT. Cell extracts were analyzed by Western blotting. ATM, ATR, CHK2, and H2AX are described in the text; CHK2 pT68, CHK2 phosphorylated on Thr^{68}; γH2AX, phosphorylated histone H2AX Ser^{139}; RPA pS4/S8, RPA phosphorylated on Ser^4 and Ser^8. (**B**) U2OS cells were treated and examined by immunofluorescence. ssDNA was detected with antibody to 5-bromo-2′-deoxyuridine. DAPI, 4′,6-diamidino-2-phenylindole. (**C**) Homologous recombination (gene conversion) was measured [(*12*); see also supporting online material]. Data from three experiments are presented as means ± SD. (**D**) U2OS survival upon CPT treatment in the presence or absence of nicotinamide. Results represent three experiments; error bars denote SD. (**E**) U2OS cells were treated as in (A) with 1 μM etoposide (ETP).

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not affect phosphorylation of CHK2 or H2AX after CPT treatment, it markedly diminished CPT-induced RPA phosphorylation and the formation of RPA and ssDNA foci, thereby mirroring the effects of nicotinamide (Fig. 2, A to C). We detected similar resection impairments with various SIRT6 siRNAs (SIRT6-1-3; fig. S4, A and B) and in different human cell types (fig. S4C). Furthermore, *Sirt6*$^{-/-}$ mouse embryonic stem cells (ESCs) were impaired in CPT-induced RPA phosphorylation (Fig. 2D). Accordingly, SIRT6 depletion reduced homologous recombination frequencies (Fig. 2E) and sensitized cells to CPT (Fig. 2F). SIRT6 depletion also rendered cells hypersensitive to inhibition of poly(ADP-ribose) polymerase (PARP; Fig. 2G), which is selectively cytotoxic to homologous recombination–deficient cells (*19*, *20*). Despite exhibiting a proficient G_2-M DNA damage checkpoint (fig. S5, A and B) presumably due to efficient CHK1 phosphorylation (fig. S5C), SIRT6-depleted cells were also hypersensitive to ionizing radiation (fig. S5D) (*18*, *21*). SIRT6 depletion had no discernible effects on cell cycle profiles (figs. S5A and S6A) or cell proliferation (fig. S6, A and B), nor did it cause pronounced apoptotic cell death (fig. S6C).

To determine how SIRT6 regulates resection, we generated stable cell lines expressing siRNA-resistant, green fluorescent protein (GFP)–tagged wild-type SIRT6 or an enzymatically inactive SIRT6 [His^{133} → Tyr (H133Y); fig. S7]. After depleting endogenous SIRT6, cells expressing wild-type but not mutant SIRT6 were proficient in CPT-induced RPA phosphorylation and formation of RPA foci (Fig. 3, A and B, and fig. S8). Thus, SIRT6 catalytic activity promotes resection-associated events. We found that SIRT6 depletion or nicotinamide treatment had no obvious effects on the levels of known DSB resection proteins and did not affect the recruitment of such proteins to DNA damage sites (fig. S9). Consistent with SIRT6 controlling resection more directly while displaying a chromatin association profile that did not alter detectably in response to CPT treatment (Fig. 3C), GFP-SIRT6 accumulated rapidly at sites of laser-induced DNA damage (Fig. 3D). These results suggested that SIRT6 might directly associate with DSB resection factors. Accordingly, when we purified GFP-SIRT6 from human cells (Fig. 3E), mass spectrometry identified the DSB resection protein CtIP. This interaction was confirmed by coimmunoprecipitation analyses [Fig. 3F; SIRT6 immunoprecipitates also contained BRCA1, a known CtIP interactor (*22*)] and appears to be direct, as indicated by assays with purified proteins (fig. S10).

The above findings led us to examine whether CtIP is acetylated. A validated pan–acetyl-lysine (AcK) antibody (fig. S11A) detected CtIP (Fig. 4A) that had been purified from human cells (fig.

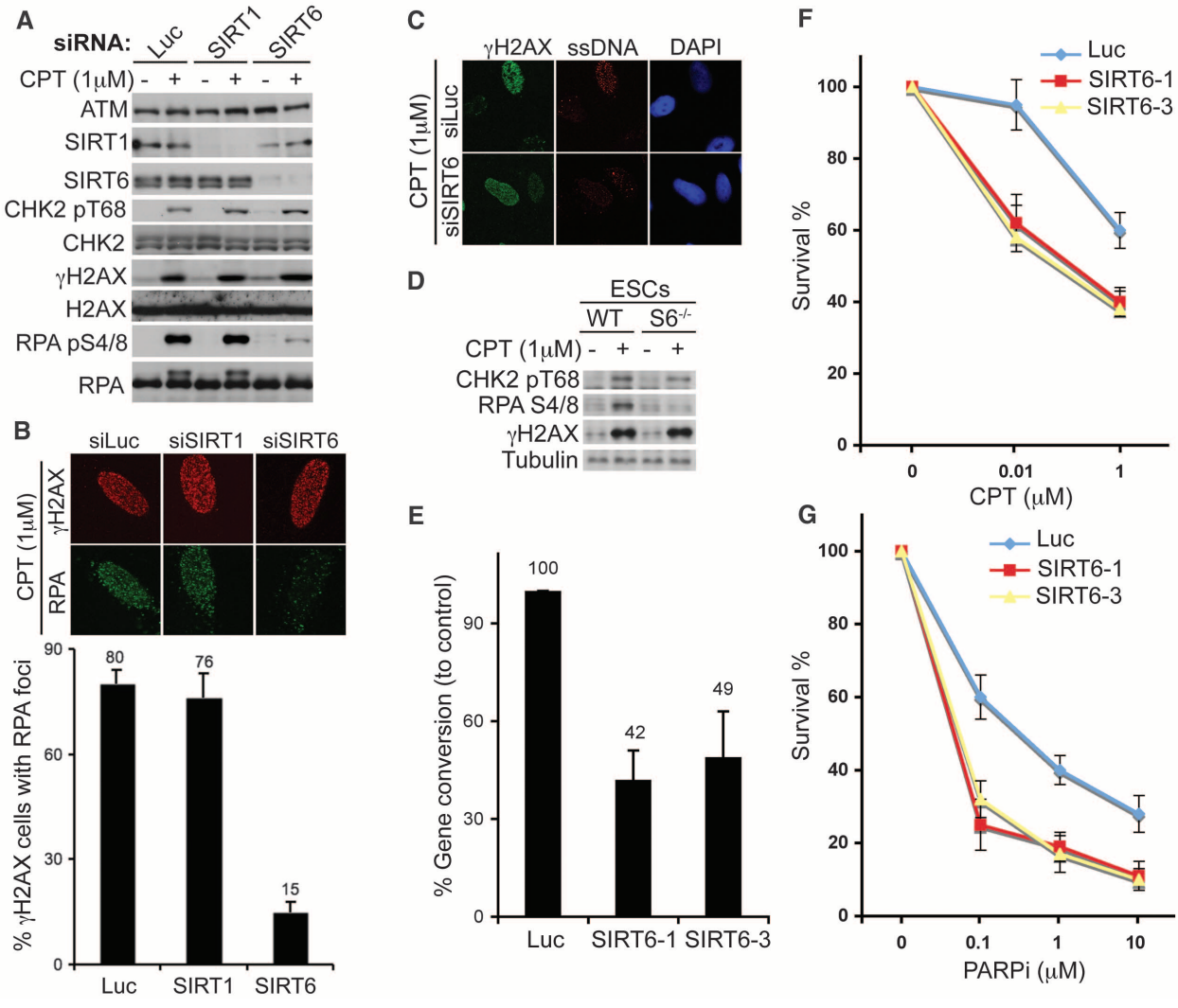

Fig. 2. SIRT6 promotes resection and homologous recombination. (**A**) SIRT1- and SIRT6- depleted U2OS cells were treated and analyzed. Luciferase siRNA (Luc) was used as control. (**B**) Upper panel: RPA immunofluorescence staining in U2OS cells after SIRT1 and SIRT6 depletion. Lower panel: Proportion of γH2AX-positive cells with RPA foci; 1000 cells were counted. (**C**) Immunofluorescence staining for ssDNA after SIRT6 depletion. (**D**) Mouse ESCs from wild-type (WT) or *Sirt6* knockout (S6$^{-/-}$) mice were treated and analyzed. (**E** to **G**) SIRT6 depletion impairs homologous recombination (E) and increases sensitivity to CPT (F) and PARP inhibitor (PARPi) (G). Data in (E) to (G) represent averages from three experiments ± SD.

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S11C). Moreover, detection by this antibody was abrogated when CtIP was treated with purified wild-type SIRT6 (fig. S11B) in the presence of NAD^+ (Fig. 4A and fig. S11C). Thus, CtIP is acetylated in a manner that can be reversed by SIRT6. Next, we assessed whether CtIP acetylation was regulated in response to DNA damage. Although we readily detected acetylation of GFP-CtIP in undamaged cells, this acetylation was abrogated if cells were treated with CPT, etoposide, or ionizing radiation (Fig. 4B; note that we ruled out the possibility that CtIP phosphorylation after DNA damage prevents detection by the AcK antibody, fig. S12A). Furthermore, DNA damage–induced deacetylation of GFP-CtIP (Fig. 4C) or endogenous CtIP (Fig. 4D and fig. S12, B to D) was blocked when cells were treated with nicotinamide or wortmannin, which inhibits the apical DNA damage response protein kinases ATM (ataxia telangiectasia mutated), ATR (ATM and Rad3 related), and DNA-PK (DNA-dependent protein kinase). [In Fig. 4D, the apparent decrease of CtIP acetylation upon DNA damage in the presence of nicotinamide reflects phosphorylation affecting CtIP mobility (*5*), as confirmed in fig. S12C.] Although SIRT6 depletion prevented CtIP deacetylation after DNA damage (Fig. 4E), this CtIP deacetylation defect was complemented by wild-type SIRT6 but not by catalytically inactive SIRT6 (Fig. 4E). Thus, CtIP is constitutively acetylated and, after DNA damage, is deacetylated by SIRT6 to promote resection. However, nicotinamide treatment did not prevent CtIP recruitment kinetics to DNA damage sites (fig. S13) or DNA damage–induced CtIP phosphorylation (Fig. 4, D and E), which suggests that deacetylation promotes the ability of CtIP to mediate resection.

When we used a recently described CtIP DNA binding mutant (*6*) where Lys^{513} and Lys^{515} were mutated to Ala (2KA), this was not detected by the AcK antibody (Fig. 4F). However, mutating these residues to nonacetylatable arginines (2KR) restored CtIP detection by the AcK antibody (Fig. 4F). This indicated that, although these positions are not sites of CtIP acetylation, the positive charge of residues 513 and 515 is required for CtIP acetylation, possibly reflecting a prerequisite for DNA binding before CtIP can access, or be recognized by, its acetyltransferase. By purifying CtIP and subjecting it to mass spectrometry, we identified several CtIP acetylation sites, of which peptides containing Lys^{432}, Lys^{526}, and Lys^{604} had highest intensity (Fig. 4G and fig. S14). Mutating these three sites to alanine (CtIP-3KA) or arginine (CtIP-3KR) markedly reduced CtIP detection by the AcK antibody (Fig. 4F). Because CtIP-3KR was effectively recruited to DNA damage sites (fig. S15A) and complemented the phenotypes caused by CtIP depletion (fig. S15A), we tested whether CtIP-3KR expression might circumvent the requirement of SIRT6 for resection. Indeed, expression of CtIP-3KR, but not of wild-type CtIP, rescued RPA phosphorylation (Fig. 4H) and formation of RPA foci in cells depleted of endogenous CtIP and SIRT6 (Fig. 4I), and also partially alleviated the homologous recombination defect of such cells (Fig. 4J). Similarly, expression of CtIP-3KR relieved the inhibitory effect of nicotinamide on RPA phosphorylation (fig. S16). These findings establish CtIP as a key SIRT6 substrate by which SIRT6 promotes resection and DSB repair by homologous recombination.

Our findings support a model in which DNA damage triggers SIRT6-dependent CtIP deacetylation, thereby promoting resection and homologous

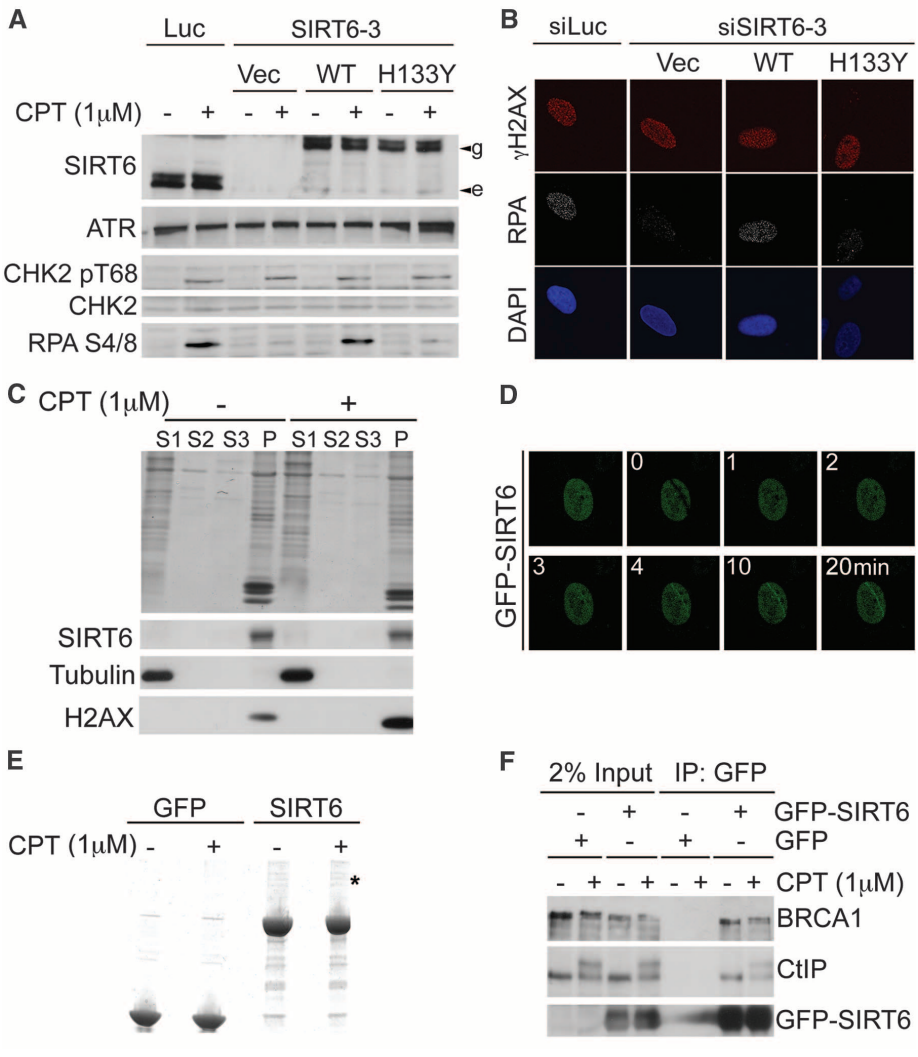

Fig. 3. SIRT6 recruitment to DNA damage sites and interaction with CtIP. (**A**) SIRT6 was depleted in U2OS cells stably expressing siRNA-resistant GFP-SIRT6 (WT or enzymatically inactive H133Y; e and g indicate endogenous and GFP-tagged SIRT6, respectively). (**B**) U2OS cells treated as in (A) were analyzed by immunofluorescence. (**C**) Fractionation of U2OS cells after CPT treatment: S1, cytoplasmic; S2, nuclear soluble; S3, 200 mM NaCl–extracted chromatin; P, pellet. (**D**) Recruitment kinetics of GFP-SIRT6 to laser-induced lesions. (**E**) Purified GFP-SIRT6 (asterisk denotes the band identified as CtIP). (**F**) Interaction between SIRT6 and CtIP by coimmunoprecipitation from U2OS cells stably transfected with GFP-SIRT6.

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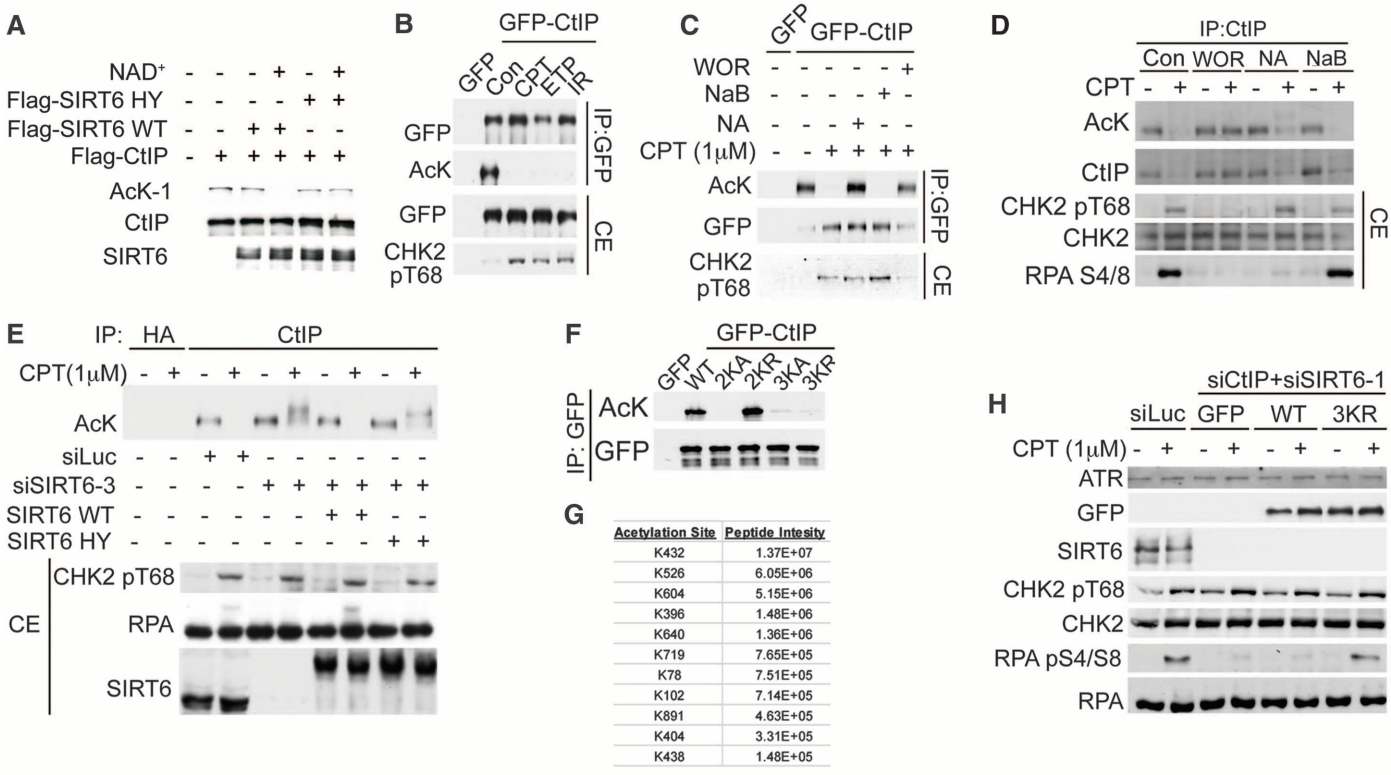

Fig. 4. SIRT6 deacetylates CtIP to promote resection and homologous recombination. (**A**) Constitutive CtIP acetylation is removed by SIRT6 in vitro after Flag-based purification from HEK293 cells. HY denotes the H133Y inactive mutant. (**B**) GFP-CtIP is acetylated in human embryonic kidney (HEK) 293 cells and deacetylated upon treatment with CPT (1 μM), etoposide (1 μM), or ionizing radiation (IR; 10 Gy). Immunoprecipitated material and cell extract (CE) were analyzed. (**C**) Nicotinamide or wortmannin (WOR) block GFP-CtIP deacetylation in HEK 293 cells after DNA damage. (**D**) Endogenous CtIP is acetylated in U2OS cells. A negative-control immunoprecipitation is shown in fig. S12D. (**E**) SIRT6 mediates CtIP deacetylation upon DNA damage. CtIP acetylation status is shown in U2OS cells stably expressing siRNA-resistant GFP-SIRT6. (**F**) Identification of CtIP acetylation sites. Mutations were introduced into GFP-CtIP and analyzed by immunoprecipitation and Western blotting. Mutants were 2KA (Lys^{513} and Lys^{515} → Ala), 2KR (Lys^{513} and Lys^{515} → Arg), 3KA (Lys^{432}, Lys^{526}, and Lys^{604} → Ala), and 3KR (Lys^{432}, Lys^{526}, and Lys^{604} → Arg). (**G**) Mass spectrometry data for intensity of acetylated CtIP peptides. (**H**) Nonacetylatable CtIP (3KR) alleviates resection defects caused by SIRT6 depletion. U2OS cells expressing siRNA-resistant GFP-CtIP (either wild-type or 3KR mutant), where SIRT6 and CtIP were depleted, were treated with CPT and analyzed. (**I**) U2OS cells treated as in (H) were analyzed by immunofluorescence. (**J**) CtIP-3KR mutant partially rescues homologous recombination defect of SIRT6-depleted cells. Cells contained vector (Vec), Flag-CtIP-WT, or 3KR. Data are from two experiments.

recombination. These results thereby establish that SIRT6 targets proteins in addition to histones (*17*, *23*), add to the known functions of SIRT6 in DNA base excision repair (*18*) and DSB repair by nonhomologous end joining (*21*), and help to explain the genome instability and premature aging phenotypes associated with SIRT6 loss in mice (*18*). Previous work has demonstrated cell cycle regulation of resection mediated via cyclin-dependent kinases regulating CtIP phosphorylation (*11*). We propose that CtIP deacetylation represents a further layer of control, presumably to ensure that resection only ensues at suitable times and locations.

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Supporting Online Material

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Materials and Methods
Figs. S1 to S16
Tables S1 and S2

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Hemocyte Differentiation Mediates Innate Immune Memory in *Anopheles gambiae* Mosquitoes

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Mosquito midgut invasion by ookinetes of the malaria parasite *Plasmodium* disrupts the barriers that normally prevent the gut microbiota from coming in direct contact with epithelial cells. This triggers a long-lived response characterized by increased abundance of granulocytes, a subpopulation of hemocytes that circulates in the insect's hemocoel, and enhanced immunity to bacteria that indirectly reduces survival of *Plasmodium* parasites upon reinfection. In mosquitoes, differentiation of hemocytes was necessary and sufficient to confer innate immune memory.

The innate immune system is thought to be hard-wired and unable to establish immunological memory (*1*). Insects lack adaptive immunity and rely on the innate immune system to mount defense responses against pathogenic organisms; however, memory-like responses have been described in invertebrates, a phenomena that has been termed immune priming (*2*). There are multiple examples of nonspecific (*3*–*5*) and pathogen-specific (*6*–*11*) priming in insects that can be long-lasting. Although these studies challenge the dogma that invertebrates are incapable of adaptive immune responses, a mechanism for innate immune memory has not been established.

Anopheles gambiae mosquitoes are the major vectors of *Plasmodium falciparum* malaria in Africa. In the present study, we found that *Plasmodium* ookinete invasion of the mosquito midgut in the presence of gut bacteria primed a robust long-lived enhanced antibacterial response that also reduced *Plasmodium* survival upon rechallenge. Immune priming resulted in quantitative and qualitative differentiation of hemocytes, the insect equivalent of white blood cells, that persisted for the lifespan of the mosquito.

We investigated the effect of preexposure of mosquitoes to *Plasmodium* infection on a subsequent infection (fig. S1) (*12*). Two groups of mosquitoes were fed on the same infected mouse. One group was placed at 28°C immediately after blood feeding, a temperature that prevents *Plasmodium berghei* ookinete formation and mosquito infection (fig. S2). We refer to these mosquitoes as the naïve group. The challenged group was kept at 21°C for 48 hours to allow ookinete formation and midgut invasion and was then switched to 28°C to reduce oocyst survival (fig. S2). Seven days postfeeding (dpf), both groups were infected by feeding on a second mouse. Reexposure to *Plasmodium* infection greatly reduced the intensity of infection in the challenged group (Fig. 1A) ($P < 0.005$). This immune enhancement was also observed in females rechallenged 14 days postpriming (dpp) ($P < 0.0005$) (Fig. 1B). The time between priming and rechallenge was not extended because of age-related mosquito mortality. Preexposure of mosquito females to *P. falciparum* (NF54 strain) infection had a similar effect, reducing oocyst density when rechallenged with the same parasite ($P < 0.05$, Mann-Whitney test) (Fig. 1C and fig. S3).

Large numbers of commensal bacteria are present in the midgut lumen when *Plasmodium* ookinetes invade epithelial cells. The blood meal is surrounded by a chitinous peritrophic matrix (PM) that normally prevents bacteria from interacting directly with epithelial cells, but ookinetes disrupt this barrier (*13*) to invade midgut cells (fig. S4), causing irreversible damage (*14*). The PM sac containing the blood-meal remnants is expelled when digestion is completed, and a new PM sac forms with each subsequent feeding. Elimination of the gut microbiota enhances *Plasmodium* infection (*15*–*17*), and activation of some mosquito antibacterial responses have been shown to indirectly kill *Plasmodium* (*17*).

Gut bacteria were eliminated by oral administration of antibiotics before the first feeding (fig. S1, yellow area), which prevented immune priming to *Plasmodium* (Fig. 1D). Then priming was allowed to occur in the presence of bacteria, but antibiotics were given 2 days before the second infection (fig. S1, beige area). Elimination of the gut microbiota when mosquitoes are rechallenged prevented elicitation of the priming response (Fig. 1E). It was the interaction between bacteria and invaded midgut cells that appeared to elicit the response, which indicates that the decrease in *Plasmodium* infection in the challenged group (Fig. 1, A and B) was not due to persistent immune activation in response to the first plasmodial infection.

The effect of priming on mosquito commensal bacteria was investigated. Total bacteria in challenged mosquitoes 7 dpp were 1% of the amount in naïve mosquitos ($P < 0.005$) (Fig. 2A). Bacterial levels in the midgut were similar between

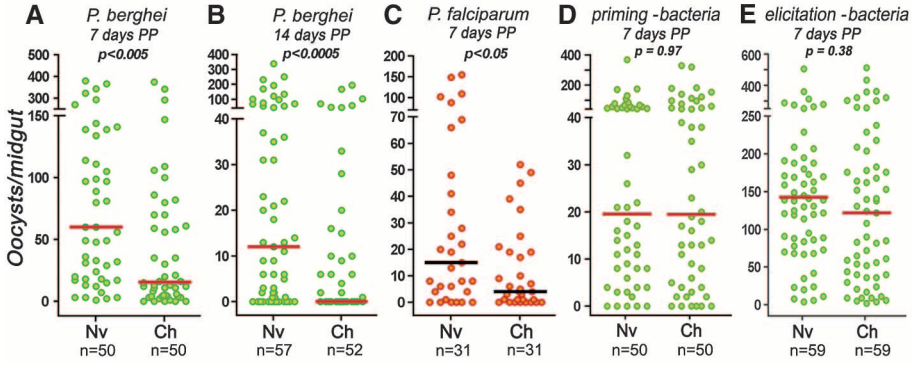

Fig. 1. Effect of preexposure to *Plasmodium* infection on the immune response to subsequent infections. (**A**) 7 dpp and (**B**) 14 dpp with *P. berghei* in naïve (Nv) or challenged (Ch) mosquitoes. (**C**) Effect of prechallenge with *P. falciparum* on a second infection at 7 dpp. *Plasmodium* infections were evaluated 7 days after the second infection. Effect of eliminating the gut microbiota with oral antibiotics before the (**D**) first and (**E**) second challenge with *P. berghei* on a second infection 7 dpp. Each circle represents the number of parasites in an individual midgut, and lines indicate the medians.

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naïve and challenged groups before the second feeding (Fig. 2B, gray). Bacteria proliferated when either naïve or challenged mosquitoes received a second meal, but bacterial levels were significantly reduced in the challenged group ($P < 0.001$) 24 hours postinfection (hpi) (Fig. 2B, blue).

No significant difference in total number of hemocytes or in relative abundance of oenocytoids (fig. S5) was observed between naïve and challenged mosquitoes 7 dpp; however, the granulocyte population increased by up to 3.2-fold (Fig. 2C) ($P < 0.01$), and prohemocytes decreased by 10% (Fig. 2D) ($P < 0.05$) in the challenged group, suggesting that prohemocyte precursors differentiated into granulocytes. This response was still present 14 dpp (fig. S6) but was no longer observed when priming was prevented by eliminating the gut microbiota (Fig. 2, C and D). Hemocytes respond to ookinete invasion by attaching to the basal surface of the midgut, which increases the mRNA levels of hemocyte-specific genes such as thioester-containing protein 1 (TEP1) and leucine-rich repeat immune protein 1 (LRIM1) associated with midguts dissected 24 hpi (*18*, *19*). This response is transient, because higher transcript levels were not detected 48 hpi (*19*). In our experiments, midgut invasion increased TEP1 and LRIM1 mRNA levels in naïve and challenged mosquitoes 24 hpi (Fig. 2E), but in challenged mosquitoes the increases in TEP1 and LRIM1 levels were up to 12- and 8-fold higher, respectively ($P < 0.005$) (Fig. 2E). As expected, a concomitant reduction in TEP1 and LRIM1 levels was observed in the population of circulating hemocytes from the same mosquitoes ($P < 0.05$) (Fig. 2E), which we speculate indicates that some hemocytes that express TEP1 and LRIM1 disappear from circulation as they attach to the midgut. This response was only observed when primed mosquitoes were reinfected, indicating an enhanced response to rechallenge rather than a persistent long-lasting response after the initial exposure to *Plasmodium* and bacteria. This enhanced hemocyte response was not observed in mosquitoes in which priming was prevented by eliminating bacteria from the gut microbiota (Fig. 2F).

Morphologic differences between granulocytes from naïve and challenged mosquitoes were apparent immediately after hemocytes were placed in plastic Neubauer chambers for counting. The cytoplasm of granulocytes from challenged mosquitoes was larger and more granular, and pseudopodial extensions were observed (Fig. 3A). However, when naïve or challenged granulocytes

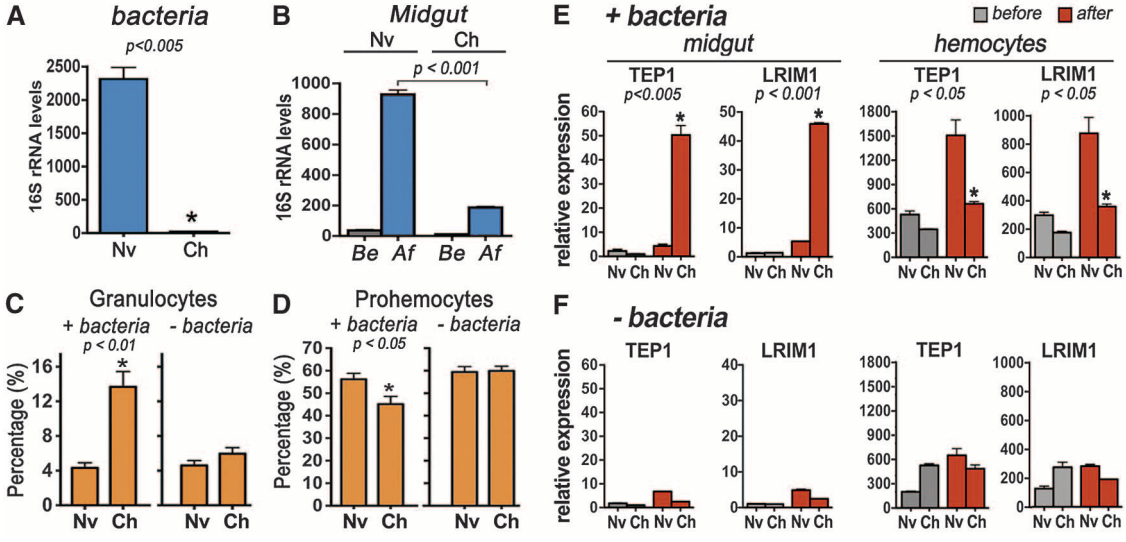

Fig. 2. Effect of immune priming with *Plasmodium* or bacteria on commensal bacteria, hemocyte populations, and gut-associated hemocyte-specific antiplasmodial mRNAs. (**A**) Effect of priming on whole-body bacterial levels in naïve (Nv) and challenged (Ch) mosquitoes 7 dpp. Bars represent mean ± SEM; asterisks indicate differences that are statistically significant (unpaired two-tailed *t* test). (**B**) Total midgut bacteria before (Be) or 24 hours after (Af) a second infectious meal was given 7 dpp. Bacterial 16*S* ribosomal RNA (rRNA) levels were determined by using real-time polymerase chain reaction (PCR). Effect of immune priming on the relative abundance of (**C**) granulocytes and (**D**) prohemocytes 7 dpp in the presence or absence of gut microbiota. Effect of immune priming on the relative abundance of TEP1 and LRIM1 mRNAs associated with the midgut or circulating hemocytes in (**E**) the presence or (**F**) the absence of gut microbiota determined before (gray) or 24 hours after (red) a second infectious meal was given 7 dpp.

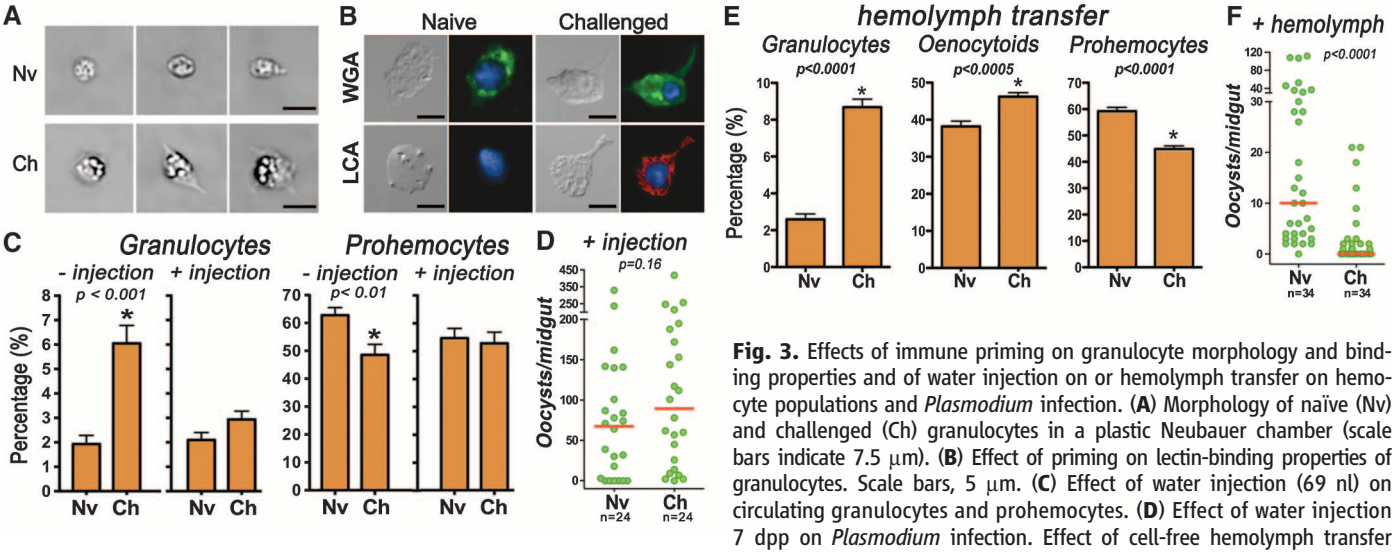

Fig. 3. Effects of immune priming on granulocyte morphology and binding properties and of water injection on or hemolymph transfer on hemocyte populations and *Plasmodium* infection. (**A**) Morphology of naïve (Nv) and challenged (Ch) granulocytes in a plastic Neubauer chamber (scale bars indicate 7.5 μm). (**B**) Effect of priming on lectin-binding properties of granulocytes. Scale bars, 5 μm. (**C**) Effect of water injection (69 nl) on circulating granulocytes and prohemocytes. (**D**) Effect of water injection 7 dpp on *Plasmodium* infection. Effect of cell-free hemolymph transfer from Nv or Ch mosquito on (**E**) circulating granulocytes, oenocytoids, and prohemocytes and (**F**) on *Plasmodium* infection 4 days posttransfer. Each circle represents the number of parasites in an individual midgut, and the line indicates the median. Bars in (C) and (E) represent mean ± SEM.

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attached to a glass surface, these morphological differences were no longer apparent (Fig. 3B). Comparison of the lectin-binding properties of naïve and challenged hemocytes to fluorescence-conjugated lectins revealed that wheat germ agglutinin (WGA) stained all hemocytes from naïve and challenged mosquitoes, including granulocytes (Fig. 3B). In contrast, only granulocytes from challenged mosquitoes were stained with *Lens culinaris* agglutinin (LCA) (Fig. 3B and table S1), whereas most (96%) of naïve granulocytes were negative and 4% were stained weakly ($P < 0.0001$; χ^2).

We disrupted granulocytes by injecting Sephadex beads resuspended in water or phosphate-buffered saline (PBS) into the hemocoel to test whether they were necessary to elicit the priming response. A control group was injected with water alone. Unexpectedly, when challenged mosquitoes were injected with a small volume of water (69 nl), the proportion of circulating granulocytes decreased to levels similar to those of naïve mosquitoes, and differences in the proportion of prohemocytes between naïve and challenged mosquitoes were no longer observed (Fig. 3C). This one-half reduction in circulating granulocytes in the challenged group is highly significant ($P < 0.0001$) and abolished priming, suggesting that these cells are necessary to elicit the priming response (Fig. 3D). Priming is also disrupted when challenged mosquitoes are subjected to aseptic injury or are injected with PBS or Sephadex beads in water (fig. S7). We speculate that primed granulocytes are probably recruited to the injury site, disappear from circulation, and are no longer available to mediate an enhanced immune response when mosquitoes are reinfected with *Plasmodium*.

Lastly, we explored whether transfer of cell-free hemolymph or hemolymph containing hemocytes from challenged mosquitoes could confer enhanced immunity in recipient mosquitoes that had only fed on sugar. Transfer of cell-free hemolymph from challenged mosquitoes by systemic injection increased the relative abundance of circulating granulocytes and oenocytoids (Fig. 3E), decreased prohemocytes (Fig. 3E), and greatly reduced both the intensity (Fig. 3F) ($P < 0.0001$) and the prevalence of *Plasmodium* infection (from 92% to 51%; $P < 0.001$; χ^2) in the recipients relative to mosquitoes that received hemolymph from naïve donors. When hemolymph containing hemocytes from challenged mosquitoes was transferred, granulocytes increased and prohemocytes were reduced in the recipients, but oenocytoids were not affected, and *Plasmodium* infection was also reduced significantly ($P < 0.0001$) (fig. S8). Transfer of cell-free hemolymph did not affect the total number of hemocytes in the recipients, but a significant reduction in circulating hemocytes ($P < 0.005$) was observed in mosquitoes that received challenged hemocytes (fig. S9). Transfer of these cells may reduce viability, proliferation, and/or adherence of endogenous hemocytes.

A strong priming response was established when ookinetes breached the gut barriers and bacteria came in contact with injured epithelial cells. The mosquito immune system was stimulated to a systemic state of enhanced immune surveillance. Upon reexposure to a similar insult, mosquitoes mounted a more effective antibacterial response that indirectly harmed *Plasmodium* parasites. We conclude that the mosquito immune system can adapt by modulating the abundance and responsiveness of different hemocyte populations. Exposure to *Plasmodium* or bacteria infection increases the proportion of circulating granulocytes and triggers changes in the morphology and binding properties of these cells. Circulating granulocytes mediate responses that enhance antiplasmodial immunity in challenged mosquitoes. Possibly, a soluble hemocyte differentiation factor(s) is released into the hemolymph of challenged mosquitoes that, when transferred, induces hemocyte differentiation in the recipients and confers enhanced antiplasmodial immunity. We propose that insect innate immune memory be defined as long-term functional changes in the immune system that allow an insect to mount a more effective immune response upon reencountering a microbe (or similar microbes). Future studies will be required to define the characteristics of this type of response and to establish how it differs from immune memory in vertebrates. Understanding the molecular mechanism(s) mediating insect immune responses such as induced hemocyte differentiation may also provide insights into the evolution of immune memory.

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Supporting Online Material

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Sequence- and Structure-Specific RNA Processing by a CRISPR Endonuclease

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Many bacteria and archaea contain clustered regularly interspaced short palindromic repeats (CRISPRs) that confer resistance to invasive genetic elements. Central to this immune system is the production of CRISPR-derived RNAs (crRNAs) after transcription of the CRISPR locus. Here, we identify the endoribonuclease (Csy4) responsible for CRISPR transcript (pre-crRNA) processing in *Pseudomonas aeruginosa*. A 1.8 angstrom crystal structure of Csy4 bound to its cognate RNA reveals that Csy4 makes sequence-specific interactions in the major groove of the crRNA repeat stem-loop. Together with electrostatic contacts to the phosphate backbone, these enable Csy4 to bind selectively and cleave pre-crRNAs using phylogenetically conserved serine and histidine residues in the active site. The RNA recognition mechanism identified here explains sequence- and structure-specific processing by a large family of CRISPR-specific endoribonucleases.

In prokaryotes, fragments of foreign DNA are integrated into clustered regularly interspaced short palindromic repeat (CRISPR) loci that are transcribed as long RNAs containing a repetitive sequence element derived from the host (*1*–*6*). These CRISPR transcripts (pre-crRNAs) are posttranscriptionally processed into short crRNAs that serve as homing oligonucleotides to prevent the propagation of invading viruses or plasmids harboring cognate sequences (*1*, *7*, *8*). CRISPR

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loci coexist with CRISPR-associated (Cas) proteins (*3*, *5*, *9*, *10*).

The opportunistic pathogen *Pseudomonas aeruginosa* UCBPP-PA14 (Pa14) harbors a CRISPR/Cas system that contains two CRISPR elements flanked by six Cas genes (Fig. 1A). Both CRISPRs comprise a characteristic arrangement of 28-nucleotide near-identical repeats interspersed with ~32-nucleotide spacers, some of which match sequences found in bacteriophages or plasmids (*11*). Processing of primary CRISPR transcripts yields crRNAs that contain one spacer sequence flanked by sequences derived from the repeat element (*1*, *2*, *12*–*15*).

To identify the protein (or proteins) responsible for producing crRNAs from pre-crRNAs in Pa14, we tested the six recombinant Cas proteins from Pa14 for endoribonuclease activity and observed sequence-specific pre-crRNA processing with Csy4 (Fig. 1B) (*16*). Csy4 did not cleave pre-crRNA from *Streptococcus thermophilus*, which has a repeat stem-loop of a distinct sequence from Pa14 (Fig. 1B). CRISPR transcript cleavage is a rapid, metal ion–independent reaction, as observed for crRNA processing within two other CRISPR/Cas subtypes (*1*, *2*).

Csy4 RNA recognition is highly specific for CRISPR-derived transcripts. When expressed in *Escherichia coli* together with a synthetic Pa14 CRISPR RNA consisting of eight repeat sequences (derived from the CRISPR locus proximal to the Cas1 ORF) and seven identical spacer sequences, Csy4 copurified with a protected ~19-nucleotide fragment derived from the Pa14 crRNA repeat (Fig. 1C and fig. S1). To explore the protein/RNA interactions required for Csy4 substrate recognition and cleavage, assays were performed in vitro by using RNA oligonucleotides corresponding to different regions of the 28-nucleotide Pa14 CRISPR repeat sequence. A 16-nucleotide minimal RNA fragment, consisting of the repeat-derived stem-loop and one downstream nucleotide, was sufficient for Csy4-catalyzed cleavage (fig. S2A). Csy4-mediated cleavage resulted in products carrying 5′-hydroxyl and 3′-phosphate (or 2′-3′ cyclic phosphate) groups, respectively (Fig. 1D).

Additionally, Csy4 activity required the presence of a 2′-hydroxyl group in the nucleotide immediately upstream of the cleavage site because 2′-deoxyribonucleotide substitution at this position abrogated cleavage but did not disrupt Csy4 binding (fig. S2). We cocrystallized Csy4 in complex with the noncleavable 16-nucleotide minimal RNA substrate in three distinct crystal forms, one containing wild-type Csy4 and two containing a catalytically active point mutant (S22C) of Csy4 (figs. S3 and S4), and solved their structures to a resolution of 2.3, 2.6, and 1.8 Å, respectively (table S1). In all three structures, the RNA binds to Csy4 in an almost identical manner, in which the protein makes extensive interactions with the single-stranded RNA (ssRNA)–double-stranded RNA (dsRNA) junction at the base of the crRNA stem as well as with the major groove of the RNA hairpin (Fig. 2A). The RNA is clamped in a highly basic groove between the main body of the protein and an arginine-rich helix (α3, residues 108 to 120) that inserts into the major groove of the hairpin (Fig. 2B).

In the complex, Csy4 adopts a two-domain architecture consisting of an N-terminal ferredoxin-like domain (residues 1 to 94) and a C-terminal domain (residues 95 to 187) that mediates most of the interactions with the RNA (fig. S5A). At the sequence level, Csy4 shares less than 10% identity with the two other known endoribonucleases involved in crRNA biogenesis, CasE from *Thermus thermophilus* (*17*) and Cas6 from *Pyrococcus furiosus* (*2*). The crystal structures of CasE and Cas6 in their nucleic acid–free states showed that these proteins possess a duplicated ferredoxin fold. The N-terminal ferredoxin fold is preserved in Csy4; structural superpositions made by using the DALI server (*18*) indicate that Csy4 in its RNA-binding conformation superimposes with CasE and Cas6 with root-mean-square deviation (RMSD) of 3.8 Å (over the N-terminal 111 Cα atoms) and 3.9 Å (over 104 Cα atoms), respectively. Although the C-terminal domain of Csy4 (residues 95 to 187) shares the same secondary structure connectivity as a ferredoxin-

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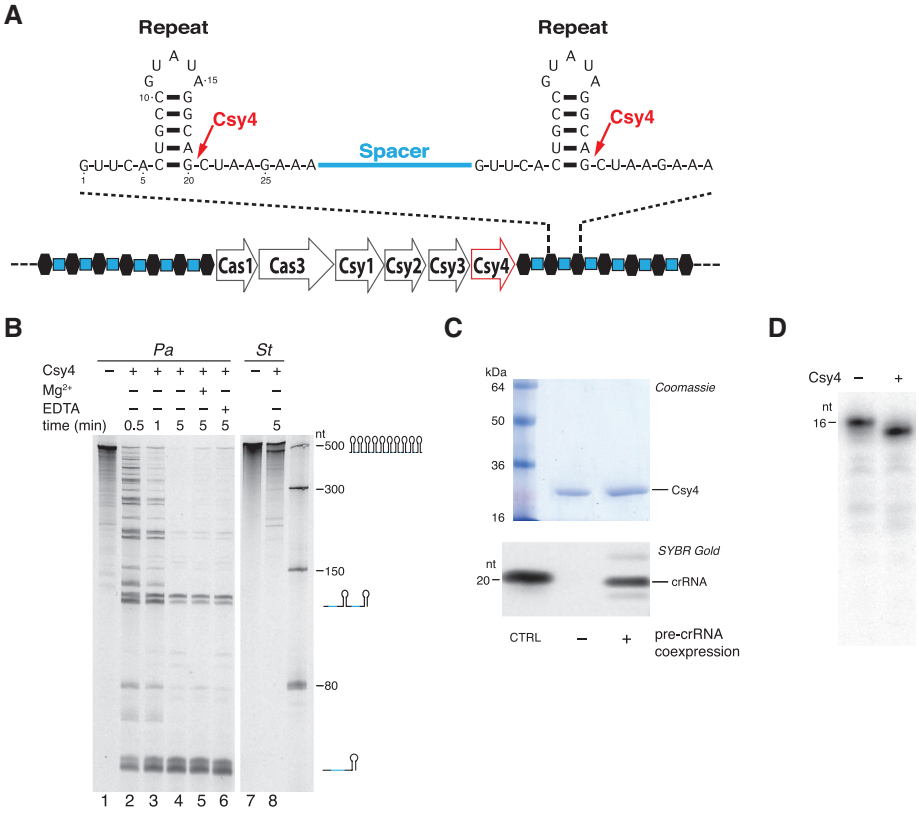

Fig. 1. Csy4 specifically cleaves only its cognate pre-crRNA substrate. (**A**) Schematic of the CRISPR/Cas locus in Pa14. The six Cas genes are flanked by two CRISPR loci, each consisting of a series of 28-nucleotide repeats (black lettering) separated by 32-nucleotide distinct spacer sequences (blue). Red arrows denote the cleavage site. (**B**) In vitro transcribed Pa14 pre-crRNA (*Pa*, lanes 1 to 6) was incubated with Csy4 in the absence of exogenous metal ions (lanes 2 to 4) or in the presence of $MgCl_2$ (lane 5) or EDTA (lane 6). *S. thermophilus* (*St*) pre-crRNA (lanes 7 and 8) served as negative control. Products were separated by means of denaturing polyacrylamide gel electrophoresis (PAGE) and visualized with SYBR Gold staining (Invitrogen, Carlsbad, CA). (**C**) Csy4 was expressed in *E. coli* in the presence (+) or absence (–) of a plasmid expressing a Pa14 CRISPR transcript. Csy4 was affinity purified; copurifying RNA was extracted and analyzed by means of denaturing PAGE and SYBR Gold staining. The ~19-nucleotide RNA corresponds to a protected fragment derived from the CRISPR repeat. (**D**) The Pa14 crRNA stem-loop (C6-G20) was 3′-end labeled using [5′-^{32}P] pCp, resulting in a minimal Csy4 substrate containing the ^{32}P radiolabel at the position of the scissile phosphate. The RNA was incubated in the presence (+) or absence (–) of Csy4. Products were separated by means of denaturing PAGE and visualized with phosphorimaging.

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like fold, its conformation is markedly different, possibly as a result of RNA binding (fig. S5B).

The crRNA substrate forms a stem-loop structure (*19*). Nucleotides 6 to 10 and 16 to 20 base-pair to produce a regular A-form helical stem. The GUAUA pentaloop contains a sheared G11-A15 base pair and an extruded nucleotide U14, which closely resembles the structures adopted by other GNR(N)A pentaloops (*20*, *21*). In the Csy4-RNA complex, the RNA stem loop straddles the β-hairpin formed by strands β6-β7 of Csy4, with the C6-G20 base pair directly stacking onto the aromatic side chain of Phe155 (Fig. 2C). In the context of the full-length CRISPR transcript, this allows Csy4 to recognize the ssRNA-dsRNA junctions in the pre-crRNA and anchor the RNA stem-loop to permit sequence-specific interactions in the major groove.

Arg102 and Gln104, located in a linker segment connecting the body of Csy4 to the arginine-rich helix, make sequence-specific hydrogen-bonding contacts in the major groove of the RNA stem to nucleotides G20 and A19, respectively (Fig. 2C). The Csy4-crRNA interaction is further stabilized by the insertion of the arginine-rich helix into the major groove of the RNA hairpin near the pentaloop (Fig. 2D). The side chains of Arg114, Arg115, Arg118, Arg119, and His120 contact the phosphate groups of nucleotides 7 to 12. Additionally, the sidechain of Arg115 hydrogen-bonds to the base of G11. The binding of the arginine-rich helix to the major groove of the crRNA hairpin is reminiscent of the N-peptide/boxB RNA interaction in lambdoid phages (fig. S6) (*22*) and of lentiviral Rev-RRE and Tat-TAR complexes (*23*, *24*).

Csy4 recognizes the hairpin element of the CRISPR repeat sequence and cleaves immediately downstream of it. In the Csy4-RNA complex structure, where RNA cleavage is abrogated by a 2′-deoxy modification in nucleotide G20, ordered electron density is only evident for the scissile phosphate between G20 and C21. The ribose and cytosine moieties of C21 are not resolved and presumably disordered. The scissile phosphate binds in a pocket located between the β6-β7 hairpin turn on one side and helix α1 on the other (Fig. 3A), hydrogen-bonding to the backbone amide of Gln149 and the side chain of His29. Ser148 is adjacent to the 2′ ribose carbon atom of nucleotide G20 (4.6 Å) and may make a hydrogen-bonding interaction with the 2′-hydroxyl group of G20 in a bona fide pre-crRNA substrate. Mutation of the strictly conserved His29 or Ser148 (to alanine and cysteine, respectively) abolished cleavage activity without disrupting RNA binding (Fig. 3B and figs. S7 and S8), suggesting that these two residues participate in catalysis. A strongly conserved tyrosine (Tyr176) is also positioned near the scissile phosphate (Fig. 3A). However, mutation of Tyr176 to phenylalanine had only a minimal effect on activity (Fig. 3B).

The requirement for a 2′ hydroxyl group in the nucleotide immediately preceding the cleavage site suggests that the catalytic mechanism of Csy4 may proceed through a 2′-3′ cyclic intermediate. In this context, the observation of an invariant serine residue (Ser148) adjacent to the 2′ ribose position upstream of the scissile phosphate is unprecedented and points to Ser148 playing a role in activating and/or positioning the 2′-hydroxyl for a nucleophilic attack on the scissile phosphate. The other functionally critical active-site residue, His29, may act as a proton donor for the 5′-hydroxyl–leaving group because mutation of His29 to lysine partially preserved catalytic activity (fig. S9).

We next tested the functional importance of Csy4 residues involved in crRNA recognition. Alanine substitution of Arg102 abolished pre-crRNA processing in vitro, whereas mutation of Gln104 to alanine did not substantially disrupt

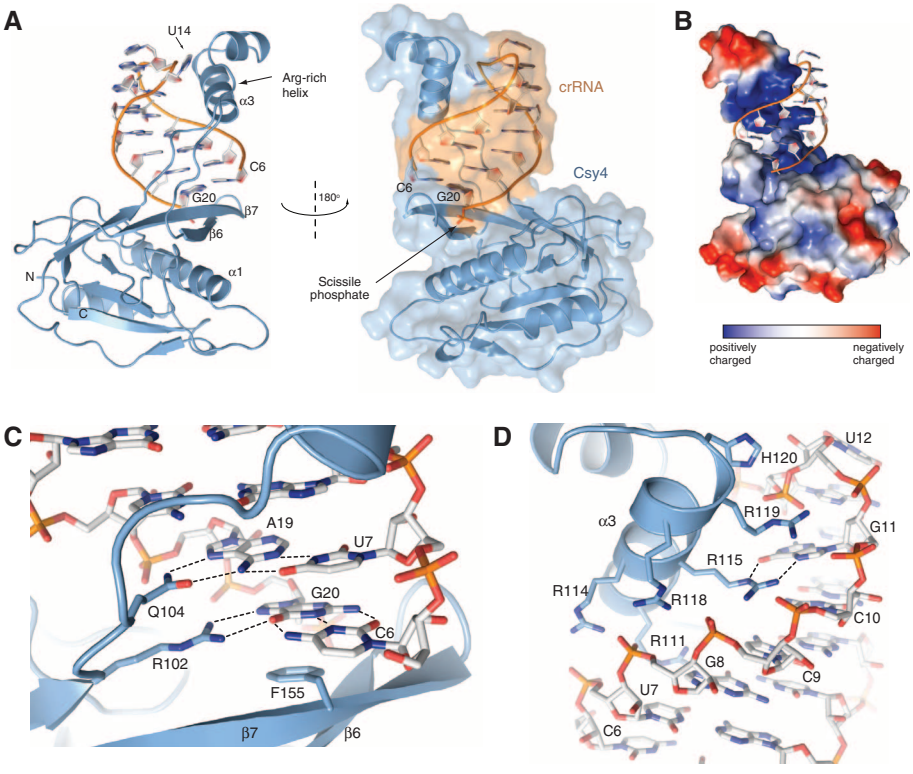

Fig. 2. The crystal structure of Csy4 bound to RNA substrate. (**A**) Front and back views of the complex. Csy4 is colored in blue, and the RNA backbone is colored in orange. (**B**) Csy4 is shown as a surface representation colored according to electrostatic potential [in the same orientation as in (A), right]. The RNA is shown in ribbon representation and colored orange. (**C**) Magnified view of the interactions between Csy4 and the major groove of the RNA hairpin. Hydrogen bonding is depicted with dashed lines. (**D**) Expanded view of the interactions between the arginine-rich helix α3 (blue) and the RNA phosphate backbone (shown in stick format, orange).

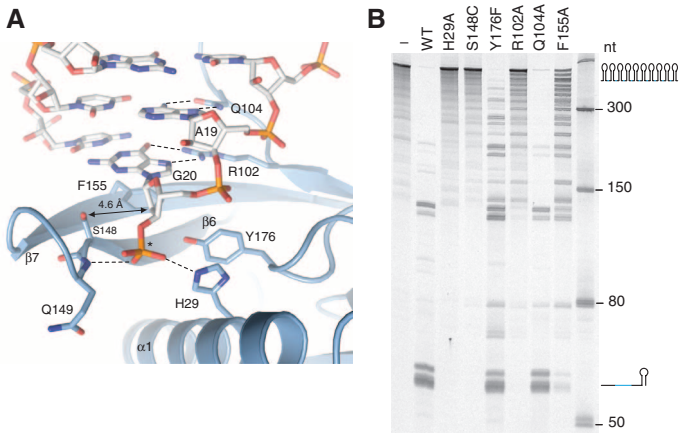

Fig. 3. Functional analysis of catalytic residues in Csy4. (**A**) Detailed view of the catalytic center. Only the phosphate group of nucleotide C21 (the scissile phosphate, indicated with an asterisk) is visible in electron density maps. Strictly conserved residues found in the proximity of the scissile phosphate are shown in stick format. The arrow indicates the distance between the hydroxyl group of Ser148 and the 2′ ribose carbon of G20. (**B**) Cleavage activity of Csy4. Wild-type (WT) Csy4 and a series of single-point mutants were incubated with in vitro transcribed pre-crRNA for 5 min at 25°C. Products were resolved by means of denaturing PAGE and visualized with SYBR Gold staining.

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activity (Fig. 3B). Mutation of Phe155 to alanine severely impaired crRNA processing, suggesting that this residue also plays an important role in substrate orientation. However, none of the above mutations severely disrupted crRNA binding, as judged by means of electrophoretic mobility shift assays, indicating that the structural integrity of the mutant proteins was not compromised (fig. S8). Thus, interaction between Csy4 and the closing base pair of the RNA stem is critical for pre-crRNA processing, whereas sequence-specific recognition of the penultimate base pair in the stem is less important. Incubation of Csy4 with a panel of short RNA oligonucleotides containing a variety of mutations in the CRISPR repeat stem-loop sequence further confirmed that Csy4 requires a C-G base pair closing the RNA stem and that Csy4 can accommodate different nucleotides at the penultimate RNA base pair (fig. S10).

Phylogenetic analysis of CRISPR loci suggests that CRISPR repeat sequences and structures have co-evolved with the Cas genes (*19*). The similarity of Csy4 at the fold level to the CRISPR-processing endonucleases CasE and Cas6 suggests that collectively they are likely to have descended from a single ancestral endoribonuclease enzyme that has diverged throughout evolution. The structure described here reveals how Csy4 and related endonucleases from the same CRISPR/Cas subfamily use an exquisite recognition mechanism to discriminate crRNA substrates from other cellular RNAs. This illustrates the importance of co-evolution in shaping molecular recognition mechanisms in the CRISPR pathway. Furthermore, the ability of Csy4 to form a tight complex with the cleaved crRNA product points to Csy4 having a functional role within the CRISPR pathway that extends beyond pre-crRNA cleavage.

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Supporting Online Material

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Prediction of Individual Brain Maturity Using fMRI

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Group functional connectivity magnetic resonance imaging (fcMRI) studies have documented reliable changes in human functional brain maturity over development. Here we show that support vector machine-based multivariate pattern analysis extracts sufficient information from fcMRI data to make accurate predictions about individuals' brain maturity across development. The use of only 5 minutes of resting-state fcMRI data from 238 scans of typically developing volunteers (ages 7 to 30 years) allowed prediction of individual brain maturity as a functional connectivity maturation index. The resultant functional maturation curve accounted for 55% of the sample variance and followed a nonlinear asymptotic growth curve shape. The greatest relative contribution to predicting individual brain maturity was made by the weakening of short-range functional connections between the adult brain's major functional networks.

Functional magnetic resonance imaging (fMRI) holds the promise that it may one day aid in the diagnosis of developmental delays and neuropsychiatric disorders, especially for conditions that lack structural brain abnormalities. Much progress has been made describing typical and atypical human brain activity at the group level with use of fMRI. However, determining whether single fMRI scans contain sufficient information to classify and make predictions about individuals remains a critical challenge (*1*).

The work described here had two major objectives. The first aim was to develop an approach for making accurate predictions about individuals on the basis of single fMRI scans. The second aim, building on the first, was to further illuminate typical brain development, a prerequisite for studying developmental disorders and pediatric-onset neuropsychiatric diseases (*2*, *3*).

Previous developmental fMRI studies have shown reliable differences between children and adults (*4*–*9*). Thus, we set out to push the study of functional brain maturation toward making predictions about single individuals. We used multivariate pattern analysis (MVPA) tools (*10*–*14*) to make continuously valued predictions about the relative functional maturity levels of individual brains.

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MVPA applies sophisticated machine-learning algorithms (*12*, *14*) to the complex patterns generated by a myriad of measurements, termed features. We chose support vector machines (SVMs) as our classification and prediction algorithms because they are resilient to overfitting and allow the extraction of feature weights (*15*, *16*). Because of its sensitivity, MVPA has become increasingly used in task-evoked neuroimaging, beginning with early work by Haxby and colleagues (*10*). When applied to task-related fMRI data, MVPA has allowed researchers to accomplish impressive feats, such as extracting patterns related to memory reinstatement (*17*), predicting which nouns participants heard (*18*), and exploring the neural correlates of consciousness (*19*, *20*).

However, in many pediatric and clinical populations, the acquisition of task-related data becomes increasingly difficult because of a variety of causes (e.g., ability to perform task). Therefore, we used functional connectivity MRI (fcMRI) data, which can be collected quickly and easily under different conditions, including but not limited to anesthesia, sleep, and quiet rest (*21*). Resting-state fcMRI (rs-fcMRI) studies measure the correlations in spontaneous activity between brain regions (*22*). These rs-fcMRI measurements are reliable across scans and institutions (*23*) and are thought to have been shaped by the cumulative effect of experiences across one's lifespan (*24*).

Thus, we developed a functional connectivity MVPA (fcMVPA) approach that combines the sensitivity of MVPA with the robust and easy data acquisition of fcMRI. To build a machine that could predict the functional maturity level of individual brains from about 5 min of fMRI data, we used 238 rs-fcMRI scans (3 T; continuous rest) from typically developing participants ranging in age from 7 to 30 years (tables S1 and S2). Blood oxygen level–dependent (BOLD) time courses were generated for 160 regions of interest (ROIs) derived from a series of meta-analyses of task-related fMRI studies that cover much of the brain (fig. S1 and table S3). All possible interregional temporal correlations, or functional connections (n = 12,720), were computed for each individual. By using standard MVPA methodology to avoid circularity bias (*14*), we first reduced the number of features to the 200 functional connections most reliably different between children and adults in each round of leave-one-out cross-validation (*16*).

Binary SVM classification of individuals as either children (61 scans of 7- to 11-year-olds; mean = 9.4) or adults (61 scans of 24- to 30-year-olds; mean = 26.2), matched for brain volume and in-scanner movement, was 91% accurate (permutation test, $P < 0.0001$; 90% sensitive; 92% specific).

To assess the relative functional brain maturity of individuals more precisely, we used SVM regression (SVR). Chronological age served as the training measure for SVR brain maturity prediction because, in contrast to other potential measures of maturity such as hormone levels or developmental milestones, age is easily obtained and free of measurement error. In this manner, we generated a predicted "brain age" as an estimate of each participants' functional maturity level. Achieving functional brain maturity in this sense is likely the consequence of integrated processes that are both developmental (e.g., myelination and synaptic pruning) and experiential.

The predicted brain ages for all scans were converted to a functional connectivity maturation index (fcMI) by setting the mean predicted brain age of typically developed young adults (18 to 30 years old) equal to 1.0. The fcMI thus represents a 200-dimensional, weighted index of an individual's overall functional brain maturity.

Model selection analyses were carried out by using Akaike information criterion (AIC) weights (*16*, *25*). These analyses showed that functional maturity levels between the ages of 7 and 30 years, as measured by fcMI, are best fit by classic biological models of asymptotic growth or maturation (*26*), such as Von Bertalanffy's growth curve or the Pearl-Reed logistic growth curve (Fig. 1 and table S4).

The most probable models of functional brain maturation provided almost identical curve fits in the 7- to 30-years-old age range (Fig. 1 and fig. S2). Linear models generated the poorest fits (fig. S2 and table S4). The best fitting models showed asymptotic maturation toward a predicted population mean maximum brain age of ~22 years, corresponding to an fcMI of slightly greater than 1.0. The fitted models mainly differed in their predictions for younger ages. The two-parameter Von Bertalanffy curve predicts more rapid maturation between birth and age 7 years than the three-parameter Pearl-Reed curve. Future collection of additional rs-fcMRI scans between birth and age 7 years should help decide between these interesting alternatives.

For independent replication, the same analyses were also carried out on two other large-scale developmental functional connectivity data sets with somewhat different characteristics. Data set 2 consisted of 195 fcMRI scans (age 7 to 31 years; 1.5 T) where rest periods had been extracted from blocked fMRI designs. Data set 3 consisted of 186 event-related fMRI scans (age 6 to 35 years) that were made more similar to resting state by regressing out task effects. Despite these differences in the type of functional connectivity data, binary adult-versus-child classification results replicated (accuracy of 92% for data set 2 and 93% data set 3), as did the functional brain maturity prediction results (data set 2, $r^2 = 0.519$; data set 3, $r^2 = 0.557$) (figs. S3 and S4, and table S4). After separately generating fcMI values for each data set, 613 scans between the ages of 6 and 30 years were combined into a single, "mixed-type" functional connectivity maturation curve (figs. S5 and S6), with very similar properties to the pure 3-T rs-fcMRI maturation curve (Fig. 1). Six participants older than 30 years from data sets 2 and 3 were excluded from the fits for consistency across data sets. These findings demonstrate that fcMRI-based maturation analyses generalize across cohorts and different types of fcMRI data.

A crucial aspect of MVPA is displaying and analyzing the features that drive the multivariate predictor. Therefore, we extracted the weighting assigned to each feature (i.e., functional connection) by the predictor and displayed the 156 consensus features (*16*) from the SVR maturity prediction (data set 1) scaled by their weights (Fig. 2 and fig. S7). The resulting pattern of feature weights verified and expanded on findings from prior developmental rs-fcMRI studies (*7*, *8*, *27*). These previous studies, which were based on smaller sets of regions and sample numbers, had suggested that the brain's functional organization is dominated by more local

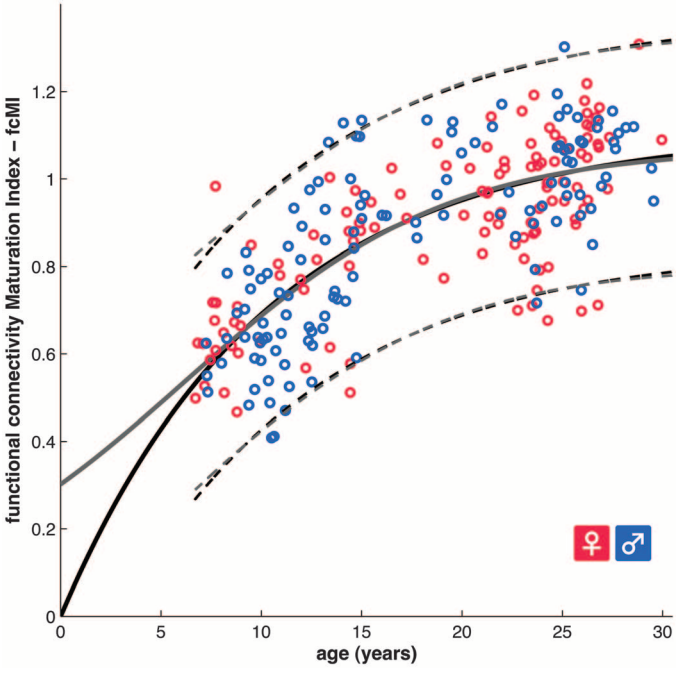

Fig. 1. Functional brain maturation curve. Individual functional brain maturity levels of 238 rs-fcMRI scans (115 females) between the ages of 7 to 30 years. Chronological age is shown on the *x* axis and the fcMI on the *y* axis (females pink, males blue). The fit for the Von Bertalanffy's equation [$a \bullet (1 - e^{-bx})$, $r^2 = 0.553$, permutation test, $P < 0.001$, AIC weight = 0.3] is shown with a solid black line. The fit for the Pearl-Reed equation [$a/(1 + b \bullet e^{-cx})$, $r^2 = 0.555$, AIC weight = 0.23] is shown with a solid gray line. The 95% prediction limits are shown with dashed lines.

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interactions between brain regions in children and shifts to a more distributed architecture in young adults.

The fcMVPA brain maturity predictor has its basis in two types of functional connections, those whose strengths were positively correlated (strengthening) with chronological age and those that were negatively correlated (weakening) with chronological age (Fig. 2, figs. S7 and S8, and table S5). As previously noted (*7*, *8*, *27*), functional connections that grew in strength across development were significantly longer (mean = 80 mm) than functional connections that diminished in strength (37 mm) [$t(154) = 14.66$, $P < 1 \times 10^{-30}$] (figs. S7 and S8). In addition, we found that functional connections increasing in strength were significantly more likely to run along the anterior-posterior (AP) axis in the horizontal plane (mean angle = 37°) than the functional connections that became weaker (58°) [$t(154) = 4.84$, $P < 1 \times 10^{-5}$]. The quantitative nature of the MVPA approach also allowed us to extract the relative contributions of weakening and strengthening functional connections. These analyses revealed that weakening connections contributed more to predicting brain maturity (68%) than strengthening connections (32%), a finding better visualized by separately summing weights for both weakening and strengthening features (Fig. 3).

To extract the relative contributions of different ROIs to maturity prediction, we computed their node or ROI weights by summing the weights across all functional connections for each ROI (Fig. 2, fig. S9, and table S6).

Some of the regions in ventromedial prefrontal cortex and parietal cortex have previously been associated with the brain's default-mode network (*28*), whereas other anterior, dorsolateral, and medial prefrontal regions are known to be important for cognitive control (*4*, *6*, *29*). Hence, we assessed the network affiliations of each ROI more formally by performing modularity optimization on the average adult functional connectivity matrix (*8*). Doing so partitioned the 160 ROIs into six networks: cingulo-opercular, frontoparietal, default mode, sensorimotor, occipital, and cerebellar (Figs. 2 and 3 and fig. S9) (*8*, *30*).

Separately summing the feature weights for each network (Fig. 3) revealed that the cingulo-opercular control network had the greatest sum total of feature weights, meaning that it was the relatively best predictor, but all six identified networks made sizeable contributions toward predicting functional maturity. Separating functional connection weights according to whether the connections occur within or between networks (Fig. 3) revealed that the vast majority of predictor weights for within-network connections were assigned to strengthening connections (Fig. 3, left). In contrast, most of the weights for between-network connections were taken up by connections that weaken (Fig. 3, right). This pattern is consistent with the internal strengthening of the adult brains' six identified major functional networks, as well as the sharpening of the boundaries between them.

The region with the greatest relative prediction power about brain maturity was the right anterior prefrontal cortex [Montreal Neurological Institute (MNI): 27, 49, 26], thought to be important for cognitive control and higher-order

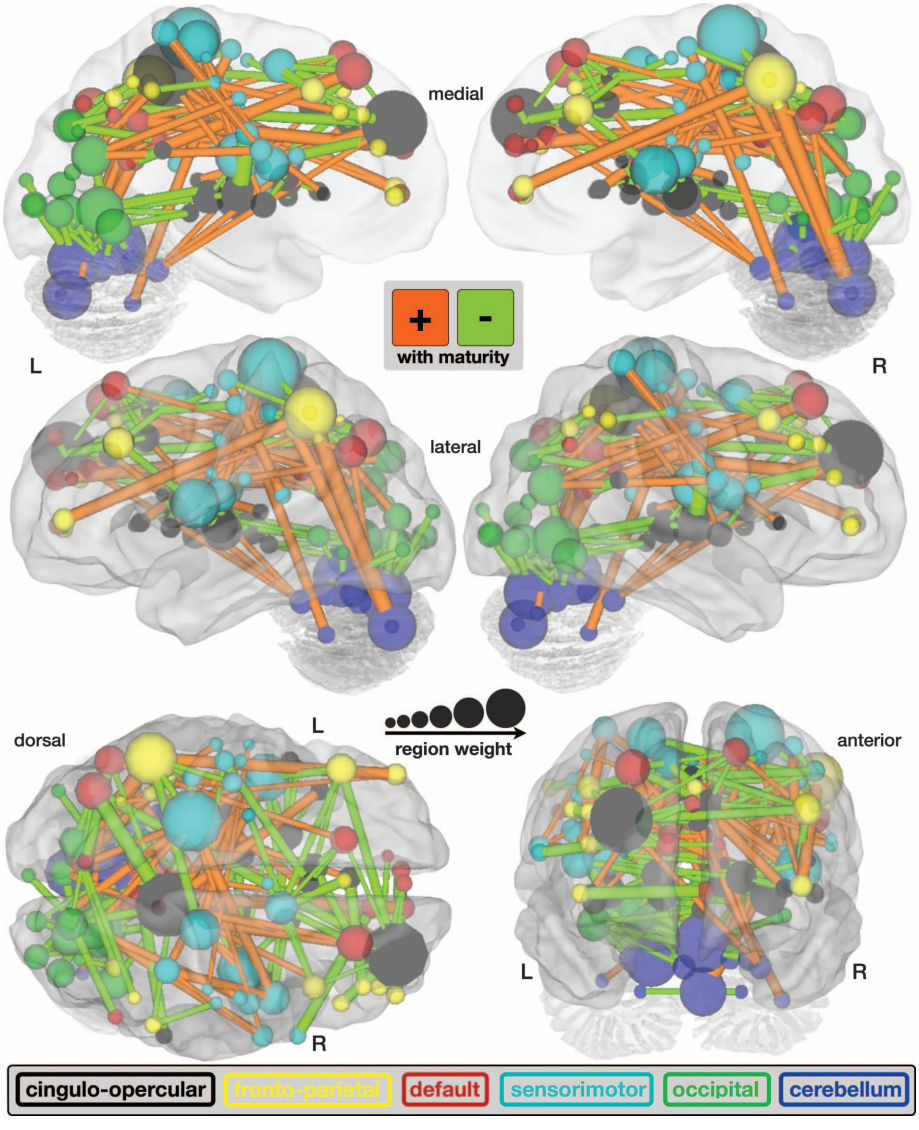

Fig. 2. fcMVPA connection and region weights. The functional connections driving the SVR brain maturity predictor are displayed on a surface rendering of the brain. The thicknesses of the 156 consensus functional connections scale with their weights. Connections positively correlated with age are shown in orange, whereas connections negatively correlated with age are shown in light green. Also displayed are the 160 ROIs scaled by their weights (1/2 sum of the weights of all the connections to and from that ROI). The ROIs are color-coded according to the adult rs-fcMRI networks (cingulo-opercular, black; frontoparietal, yellow; default, red; sensorimotor, cyan; occipital, green; and cerebellum, dark blue).

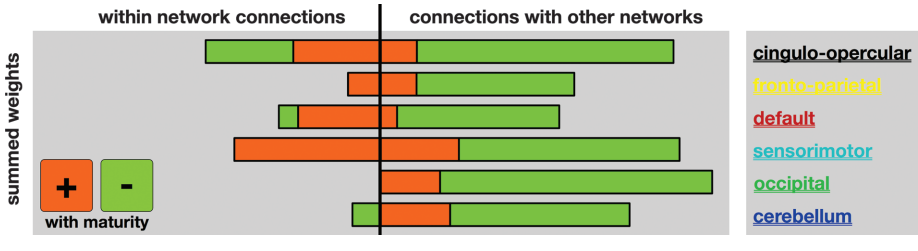

Fig. 3. SVR brain maturity weights by adult rs-fcMRI networks. The sums of all the functional connection weights within each network are shown to the left of the vertical black line. The sums of all the functional connection weights between networks are shown to the right.

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reasoning (*4*, *6*, *9*, *29*). The precuneus, which has recently been found to be the most highly structurally (*31*) and functionally (*32*) connected brain region, contained the second most predictive ROI (MNI: 8, –40, 50). It stands to reason that regions such as those in the precuneus, situated at the center of the adult brain's connectome, could carry much information about how the network develops.

The results presented here strongly suggest that the fcMVPA approach derives its accuracy from important neurophysiologic changes. The functional connectivity maturation curve (Fig. 1 and fig. S6) has a biologically plausible asymptotic shape, first used to describe the growth of animals (Von Bertalanffy) and human populations in the setting of limited resources (Pearl-Reed) (*26*). Similarly shaped growth curves that plot measures such as height and head circumference against age are used routinely in pediatric medicine. The maturation curves suggest that mean population functional brain maturity asymptotes toward a maturity level or brain age of ~22 years (*33*). The shape of the functional maturation curve highlights the nonlinear nature of functional brain maturation (*34*, *35*).

The pattern of fcMVPA feature weights indicated that functional maturation is driven both by the segregation of nearby functional areas, through the weakening of short-range functional connections, and the integration of distant regions into functional networks, by strengthening of long-range functional connections (fig. S7) (*2*, *7*, *8*, *27*). It is interesting that fcMVPA revealed the relatively greater importance of functional segregation when compared to functional integration for the prediction of functional brain maturity. In addition, fcMVPA showed that functional integration is mainly carried by longer-range functional connections along the AP axis. Grouping brain regions into functional networks (*8*) showed that both integration within functional networks and segregation between them are widely distributed across the cortex and cerebellum.

Several important, large-scale structural MRI studies of brain maturation have already mapped out anatomical maturation curves for a variety of measures (*33*, *34*, *36*, *37*). The present study provides a functional counterpart to the prior anatomical studies. In addition, it combines the most relevant features into a single index instead of separately listing different measures. It should be informative to apply similar MVPA methods to the study of structural brain maturation, as well as combining MVPA of structural and functional data.

Important group-level rs-fcMRI studies have already shown differences in spontaneous activity in disorders such as autism, schizophrenia, depression, and attention-deficit hyperactivity disorder (*21*). Hence, imaging-based binary classification studies of clinical populations are starting to be pursued (*38*). The use of SVR in fcMVPA to make continuously valued predictions may become relevant in clinical scenarios where binary classification is insufficient (e.g., to predict years until Alzheimer's disease symptom onset).

The standard clinical workup for many developmental neuropsychiatric disorders already includes a structural MRI scan of the brain. The present observations suggest that the addition, at little extra cost, of a brief resting acquisition to the standard clinical study could one day provide useful information to aid in the screening, diagnosis, and prognosis of individuals with disordered brain function.

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Supporting Online Material

www.sciencemag.org/cgi/content/full/329/5997/1358/DC1
Materials and Methods
SOM Text
Figs. S1 to S9
Tables S1 to S6
References

23 June 2010; accepted 4 August 2010
10.1126/science.1194144

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Gordon Research Conferences

frontiers of science

2011 "Session I" Meeting Schedule and Preliminary Programs

Photo: *Sea ice near the edges of the Amundsen Sea Polynya in the South Pacific Sector of the Antarctic. (Photo credit: Patricia Yager, Chair, Polar Marine Science GRC). The Polar Marine Science GRC and its accompanying Gordon Research Seminar will take place in March 2011 at the Four Points Sheraton in Ventura, California.*

2011 "Session I" Meetings will be held between January and May in Ventura, California and Galveston, Texas in the United States; and internationally in Italy and Switzerland. A list of preliminary programs appears on the following 10 pages. For detailed programs, fees, site/travel information and online application, visit our web site at **www.grc.org**.

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NEW! ***Introducing:*** **Gordon Research Seminars**

Gordon Research Seminars (GRS) *are 2-day meetings that precede a corresponding GRC. They provide a unique opportunity for* ***graduate students, post-docs and other young investigators*** *to share in the GRC experience. 13 Gordon Research Seminars will be held during Session I in 2011. The preliminary program for each GRS appears with its corresponding GRC in the listings on the following pages.*

The Benefits of a GRS:

- **Network with your peers** in an informal atmosphere
- **Engage in scientific discussions** at the forefront of your field
- **Interact with leaders** who may serve as mentors during your career
- **Gain the confidence to participate in a Gordon Research Conference** - apply to both the GRS & GRC

Contribute to a GRS:

- **Submit an abstract** - abstracts are used to select speakers
- **Present a poster** and get valuable feedback and suggestions

visit the frontiers of science. . . go to a gordon conference! (www.grc.org)

The list of meetings, topics and speakers begins below (discussion leaders are noted in italics). Gordon Research Seminars (GRS) are listed below their associated Gordon Conference.

ANTIMICROBIAL PEPTIDES

Antimicrobial Peptides in Innate Immunity - New Insights on an Ancient System
May 15-20, 2011
Il Ciocco Hotel and Resort, Lucca (Barga), Italy
Chairs: Jens Schroeder & Birgitta Agerberth
Vice Chairs: Gill Diamond & Nita H. Salzman

- **Keynote Session: AMPs - Novel Knowledge of an Ancient Defense System** (*Jens Schroeder, Birgitta Agerberth* / Thomas Bosch / Robert Hancock)
- **Antimicrobial Peptides: Diversity and Phylogenetics** (*Charles Bevins* / Mohamed A. Marahiel / Theresa L. Chang / Matthias Leippe)
- **Other Functions of AMPs and Non-AMPs with Antimicrobial Activity** (*Andy Ouellette* / Tetsuya Higashiyama / Oliver Soehnlein)
- **Regulation of AMP Synthesis** (*Ylva Engström* / Michael Hoch / Manuela Raffatellu / Rubhana Raqib)
- **Microbial Responses and Resistance to AMPs** (*Hans-Georg Sahl* / Christoph Ernst / Konstantin Severinov / Tanja Schneider)
- **Structural and Functional Parameters of AMP Action** (*Margitta Dathe, Gill Diamond* / Yechiel Shai)
- **AMPs in Host-Microbe and Microbe Interaction** (*Pieter Hiemstra* / Peter Mergaert / Nita Salzman / Richard Gallo / Tadayuki Iwase)
- **AMPs in Health, Disease and Beyond** (*Robert Bals, Paul McCray* / Arturo Zychlinsky / Vojo Deretic / Charles Esmon / Jan Wehkamp)
- **AMPs: From Bench to Application** (*Michael Zasloff, Mona Stahle* / Colin Hill / Hans-Henrik Kristensen / Michael Kleine)

CANCER GENETICS & EPIGENETICS

Jan 23-28, 2011
Ventura Beach Marriott, Ventura, CA
Chairs: Kristian Helin & Bruno Amati
Vice Chair: Joseph F. Costello

- **Keynote Session: The Genetic and Epigenetic Pathways of Cancer** (*Kristian Helin* / Joe Gray / Frank McCormick / Peter A. Jones)
- **Genetic and Molecular Alterations in Cancer I** (*Joseph Costello* / James R Downing / A. Thomas Look / Richard Houlston)
- **Genetic and Molecular Alterations in Cancer II** (*Karen Cichowski* / Pier Giuseppe Pelicci / Katherine A Jones)
- **Integrative Cancer Genetics and Epigenetics** (*Katerine A. Jones* / Joseph Costello / Jean-Pierre Issa / Karen Cichowski)
- **Cancer Epigenomics** (*Gigi Lozano* / Peter Laird / Susan Clark)
- **Mouse Models for Cancer** (*Susan Clark* / Anton Berns / Gigi Lozano / Alan R. Clarke)
- **The Role of ncRNA in Cancer** (*Joseph R. Nevins* / Carlo Croce / Frank Slack)
- **Cancer Transcriptome and Genome Profiling** (*En Li* / Joseph R. Nevins / Vessela Kristensen / Michael R. Stratton)
- **Novel Targeted Anti-Cancer Therapies** (*Bruno Amati* / En Li / Frederic J. De Sauvage / Ricky Johnstone)

CANNABINOID FUNCTION IN THE CNS

May 22-27, 2011
Les Diablerets Conference Center
Les Diablerets, Switzerland
Chairs: Beat Lutz & Vincenzo Di Marzo
Vice Chairs: Andrea Hohmann & David Lovinger

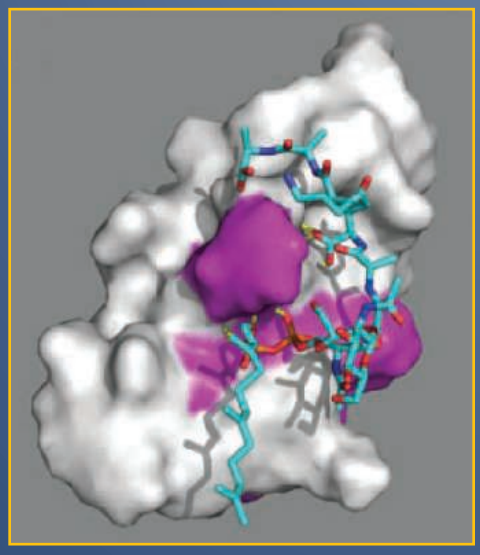
- **Keynote Presentation: Neuron Glia Metabolic Coupling and Plasticity** (Pierre Magistretti)
- **Chemical and Genetic Tools Targeting the Endocannabinoid System** (*Daniele Piomelli* / Didier Lambert / Ben Cravatt / Patrick Doherty)
- **Phytocannabinoids and Endocannabinoid-Like Molecules in the Brain** (*Raphi Mechoulam* / Roger Pertwee / Francoise Rohner-Jeanrenaud / Pier Vincenzo Piazza)
- **Endocannabinoids in Synaptic Processes and Neuronal Circuits** (*Ivan Soltesz* / Brad Alger / Masanobu Kano / Robert Malenka)
- **Endocannabinoids in Neurogenesis, Cell death, and the Establishment of Neuronal Circuits** (*Ken Mackie* / Tibor Hakany / Rainer Glass)
- **Endocannabinoids in Neuron-Glial Interaction, Neuroinflammation and Energy Metabolism** (*Pierre Magistretti* / Nephi Stella / Giovanni Marsicano / Jaideep S. Bains / Alfonso Araque)
- **Endocannabinoids and the Control of Cognition, Emotionality and Reward** (*Maria-Paz Viveros* / Miriam Schneider / Gabriella Gobbi / Miriam Melis)
- **Endocannabinoids in Neurological Disorders** (*Manuel Guzman* / Mauro Maccarrone / Javier Fernandez-Ruiz / Anatol Kreitzer)
- **Endocannabinoids and the Spinal and Supra-Spinal Control of Pain** (*Andrea Hohmann* / Sabatino Maione / Andreas Zimmer / Victoria Chapman)

NEW! CANNABINOID FUNCTION IN THE CNS (GRS)

Dysregulation of the Endocannabinoid System and Ensuing Pathological States
May 21-22, 2011
Les Diablerets Conference Center
Les Diablerets, Switzerland
Chair: Sabine Ruhle
Associate Chair: Krisztina Monory

The Gordon-Kenan Research Seminar on Cannabinoid Function in the CNS is a unique forum for graduate students, post-docs, and other scientists with comparable levels of experience and education to present and exchange new data and cutting edge ideas. The focus of this meeting is to discuss the anatomical and cellular complexity of the endocannabinoid system and to detail dysregulations under pathophysiological states in order to inspire novel therapeutic approaches to alleviate ailments. This GRS will also address innovative techniques for the analysis of the endocannabinoid system.

- **Speakers:** To be selected from submitted abstracts
- **Discussion Leaders:** To be selected from submitted abstracts
- **Keynote Speakers:** Nephi Stella
- **Mentorship Component:** "Guidance in the Jungle of Science and Scientists", featuring Ken Mackie and Betty Yao



The fungal defensin Plectasin targets the bacterial cell wall precursor Lipid II. NMR-based model of the plectasin/lipid II-complex: Surface representation of plectasin with the residues showing substantial chemical shift perturbation upon lipid II titration, which is shown in magenta. Courtesy of Tanja Schneider *et al* (originally published in *Science* 328, 1168- 1172, 2010). Submitted by Jens Schroeder, Chair, Antimicrobial Peptides GRC. Tanja Schneider is an invited speaker at the conference.

CARDIAC ARRHYTHMIA MECHANISMS

Systems Approaches to Cardiac Arrhythmia Research
Feb 13-18, 2011
Hotel Galvez, Galveston, TX
Chair: James N. Weiss
Vice Chair: Mario Delmar

- **State-of-the-Art and Coming Attractions in Clinical Arrhythmia Management** (*Douglas Zipes* / William Stevenson / Henry Halperin / Natalia Trayanova)
- **Systems Approaches to Cardiac Arrhythmias** (*Andrew McCulloch* / Emelia Benjamin / Jennifer Van Eyk / Stanley Nattel / Howard Rockman)
- **What Makes Atria Fibrillate?** (*Daniel Roden* / Jose Jalife / Xander Wehrens / Nipavan Chiamvimonvat)
- **Ca Cycling and Arrhythmias: Alternans, Afterdepolarizations and CPVT** (*David Rosenbaum* / Sandor Gyorke / Bjorn Knollman / Wayne Chen)
- **Arrhythmias in Diseased and Failing Hearts** (*Mark Anderson* / Zhilin Qu / C. Cabo / Igor Efimov)
- **Ion Channel Interacting Proteins and Arrhythmias** (*Guy Salama* / Peter Mohler / Justus Anumonwo / Robin Shaw / Connie Bezzina)
- **Fibrosis and Arrhythmias** (*Stephan Rohr* / Stefan Englehardt / Peter Kohl / Heather Duffy)
- **Channelopathies and Arrhythmias** (*Coleen Clancy* / Charles Antzelevitch / Yoram Rudy / Gideon Koren / Carlo Napolitano)
- **The Conduction System, Pacemaking and Biological Pacemaker Design** (*Peng-Sheng Chen* / Glenn Fishman / Edward Lakatta / Vadim Fedorov / Michael Rosen)

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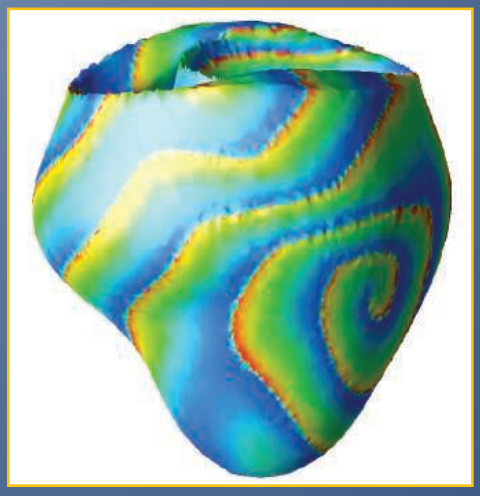

Scroll wave reentry simulating sudden cardiac death. Courtesy of A. Garfinkel & colleagues. Submitted by James N. Weiss, Chair, Cardiac Arrhythmia Mechanisms GRC.

CARTILAGE BIOLOGY & PATHOLOGY

Mar 6-11, 2011
Ventura Beach Marriott, Ventura, CA
Chairs: Karen M. Lyons & Kathryn Song Eng Cheah
Vice Chairs: Rocky S. Tuan & Andrea Vortkamp

- **Development / Evolution of Cartilage**
  (*Andrea Vortkamp* / Shigeru Kuritani / Rich Schneider)
- **Signaling and Control Mechanisms**
  (*Ernestina Schipani* / Veronique Lefebvre / Matthew Hilton / Xiangli Li)
- **Genetic Analysis of Skeletal and Metabolic Disorders**
  (*Bjorn Olsen* / Henry Kronenberg / Brendan Lee / Deborah Krakow)
- **Chondrocyte Polarity and Cytoskeletal Control**
  (*Philip Beales* / Yingzi Yang / Kevin Jones)
- **Cellular Stress in Cartilage**
  (*Linda Sandell* / Hiroshi Asahara / Hiroshi Kawaguchi / Frank Beier)
- **Stem Cells and Cartilage Degenerative Disorders**
  (*Danny Chan* / Mak Risbud / Ben Alman / Thomas Papp)
- **Inflammatory Mechanisms in Cartilage Maintenance and Degeneration**
  (Konstantin Taganov / Hsing-Jung (Joyce) Wu / Ru Liu-Bryan)
- **Cartilage Repair, Regeneration, and Tissue Engineering**
  (*Rocky Tuan* / Vicki Rosen)
- **Enabling Technologies for Cartilage Research**

CELL BIOLOGY OF MEGAKARYOCYTES & PLATELETS

Mar 20-25, 2011
Hotel Galvez, Galveston, TX
Chair: Mortimer Poncz
Vice Chair: Katya Ravid

- **Stem Cells and Megakaryocyte Potential During Embryogenesis**
  (*Merv Yoder* / James Palis / Najet Debili / Paul P. Liu)
- **Transcription Factors, miRNAs and other Regulators of Megakaryopoiesis**
  (*Gerd Blobel* / Alan Cantor / Diane Krause)
- **Regulatory Pathways Affecting Polyploidy and Megakaryocyte Maturation**
  (*William Vainchenker* / Alessandra Balduini / Stephen Nimer)
- **When Megakaryocytes Go Bad: Lessons from Down Syndrome and Myelo-Proliferative Disorders**
  (*John Crispino* / Stella Chou / Ross Levine)
- **Thrombopoiesis: Where, When and What?**
  (*Joe Italiano* / Walter Kahr / Martha Sola-Visner)
- **New Insights from New Players in Platelet Biology**
  (*Steve Watson* / Yotis Senis / A. Valance Washington / Sandford Shattil)
- **New Insights from Old Players in Platelet Biology**
  (*Peter Newman* / Deborah Newman / Mark Kahn)
- **Lessons from Megakaryocyte/Platelet Genomics and Proteomics**
  (*Daniel Simon* / Leslie Parise / Wadie F. Bahou / Daniel Simon)
- **New Approaches to Controlling Activated Platelets**
  (*Douglas Cines* / Thomas Wisnewski)

NEW! CELL BIOLOGY OF MEGAKARYOCYTES & PLATELETS (GRS)

Establishing a Research Career in Platelet Biology and Hemostasis/Thrombosis

Mar 19-20, 2011
Hotel Galvez, Galveston, TX
Chair: Donald J. McCrann
Associate Chair: Rudy Fuentes

The Gordon-Kenan Research Seminar on Cell Biology of Megakaryocytes & Platelets is a unique forum for graduate students, post-docs, and other scientists with comparable levels of experience and education to present and exchange new data and cutting edge ideas. The focus of this meeting is on the brightest young investigators in the fields of megakaryopoiesis and platelet biology and their latest advances in understanding megakaryocyte and platelet formation and function in hemostasis/thrombosis. Through career oriented presentations and a round table discussion with both academic and pharmaceutical leaders in this field, this GKRS will also provide young researchers with valuable career advice from experts conducting basic, translational and pharmaceutical research.

- **Speakers:** To be selected from submitted abstracts
- **Discussion Leaders:** Katya Ravid, Mitch Weiss, and Barry Coller
- **Keynote Speakers:** Barry Coller and Elliot Barnathan
- **Mentorship Component:** "Career Development in Cell Biology of Megakaryocytes and Platelets", a Career Panel featuring Elliot Barnathan, Mortimer Poncz, Katya Ravid, Mitchell Weiss, and Barry Coller

CHEMICAL & BIOLOGICAL TERRORISM DEFENSE

Basic Science as a Foundation for the Development of Countermeasures

Mar 20-25, 2011
Ventura Beach Marriott, Ventura, CA
Chair: Molly A. Hughes
Vice Chair: Keith B. Ward

- **Keynote Presentation: Synthetic Genomics and Bioethics in Biodefense Research**
  (*Drusilla Burns, Stephen Morse* / Arthur Caplan)
- **Viral Pathogens - Pathogenesis, Detection, and Treatment**
  (*Peter Jahrling* / Dennis Hruby / Gerd Sutter / Jeffrey Taubenberger / Ralph Baric)
- **Genetics and Genomics of Biodefense-Related Pathgoens**
  (*Richard Rest, Jeff Miller* / Theresa Koehler / William Nierman / Petra Oyston)
- **Host-Microbe Interactions: Immune Suppression / Evasion**
  (*Arturo Casadevall* / W. Joost Wiersinga / Cosima Baldari / James Bliska)
- **An Inside Job: How Intracellular Pathogens Exploit and Remodel Host Cells to Establish Residence, Subvert Host Defense, and Promote Transmission**
  (*Steven Blanke* / Jean Celli / Michele Barry / Geoffrey Smith)
- **Chemical Defense and Cutting Edge Research Developments**
  (*Rudolph Johnson* / Clem Furlong / Mark Kirk / Ronald Evans / Karen Wahl)
- **Select Poster Abstract Presentations**
  (*David Relman*)
- **Agricultural Agents of Bioterrorism: Plant Pathogens**
  (*Jacqueline Fletcher* / Adam Bogdanove / Sophien Kamoun / Jan Leach / June Medford)
- **Cutting Edge Therapeutic Strategies for Biodefense Agents**
  (*Randall Kincaid* / Ronald Germain / Patrick Iversen / Nicolas Valiante)

NEW! CHEMICAL & BIOLOGICAL TERRORISM DEFENSE (GRS)

Research Frontiers in Chemical and Biological Defense

Mar 19-20, 2011
Ventura Beach Marriott, Ventura, CA
Chair: Matthew Crawford
Associate Chair: Stephanie Rogers

The Gordon-Kenan Research Seminar on Chemical & Biological Terrorism Defense is a unique forum for graduate students, post-docs, and other scientists with comparable levels of experience and education to present and exchange new data and cutting edge ideas. The focus of this meeting is on basic and translational research advances in the field of chemical defense and biological defense of humans, animals, and plants. Seminar and poster sessions will reflect the multi-disciplinary nature of this field and will cover topics including molecular mechanisms of pathogenesis and toxicity, host-microbe interactions, innate host response, advances in detection capabilities, and countermeasure development.

- **Speakers:** To be selected from submitted abstracts
- **Discussion Leaders:** David Lowe and Ian Gut
- **Keynote Speakers:** "Advances in Synthetic Biology and Implications for Biodefense", Speaker TBA

CHEMICAL REACTIONS AT SURFACES

Feb 6-11, 2011
Ventura Beach Marriott, Ventura, CA
Chair: Michael A. Henderson
Vice Chair: Peter C. Stair

- **Keynote Presentation: Molecular Studies of Catalytic Selectivity of Metal Nanoparticles under Reaction Conditions - New Instrumentation and Evolution of Concepts**
  (*Peter Stair* / Gabor Somorjai)
- **Catalysis at Metal Surfaces**
  (*Janice Reutt-Robey* / Eddy Tysoe / Wayne Goodman / Jason Weaver)

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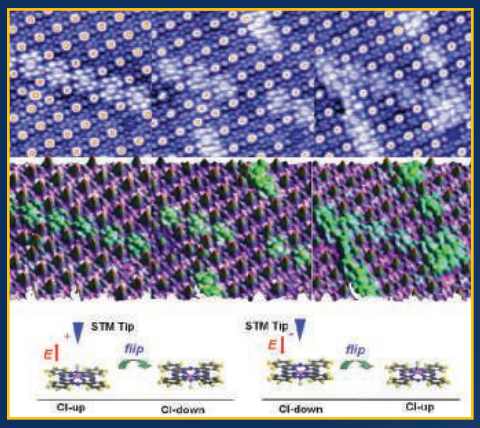
- **Energy Conversion at Surfaces**
  (*Christof Wöll, Zdenek Dohnalek* / Karina Morgenstern / Kazunari Domen / Dave Dixon / Nenad Markovic)
- **Hydrogen Production and Separation at Surfaces**
  (*Levi Thompson* / Anders Nilsson / Andy Gellman / Mike Bowker)
- **Interfacial Chemistry in Photovoltaics**
  (*Jason Baxter* / Stacy Bent / Andrew Wee)
- **Liquids at Surfaces**
  (*Miquel Salmeron* / Bruce Kay / Hans-Peter Steinrück)
- **Chemical Reactions at Oxide Surfaces**
  (*José Rodriquez* / Judith Yang / Mike Bedzyk / Susannah Scott)
- **Surface Chemistry of CO_2 Conversion**
  (*Bill Schneider* / Eric Altman / Jens Nørskov)
- **Hot Topics in Surface Chemical Reactions**
  (*Buddie Mullins*)



The letter 'N' is written on a molecular dipole monolayer on graphite surface via single-molecule manipulation. Reversible transformations of the ClAlPc (chloroaluminum phthalocyanine) molecular configuration in the close-packed layer can be controlled by bias-voltage pulses applied to the STM tip. Courtesy of Andrew Wee, National University of Singapore. Submitted by Michael A. Henderson, Chair, Chemical Reactions at Surfaces GRC.

CILIA, MUCUS & MUCOCILIARY INTERACTIONS

Feb 13-18, 2011
Ventura Beach Marriott, Ventura, CA
Chairs: Mary C. Rose & Burton F. Dickey
Vice Chairs: Stephen M. King & Martina Brueckner

- **Towards Integrating Cilia, Mucins and Mucociliary Interactions: Prospects and Themes**
  (*Peter Satir, Sandra Gendler* / Gregory Pazour / David Thornton / Richard Boucher)
- **Development of Cilia and Secretory Cells**
  (*Mary Porter* / Maxance Nachury / Christopher Kintner / Steven Brody / Wellington Cardoso / Jeffrey Whitsett / Scott Randell)
- **Signaling and Regulation of Cilia and Mucins**
  (*Reen Wu, Susan Dutcher* / Wallace Marshall / Zhaoxia Sun / Isabelle Van Seuningen / Christopher Evans)
- **Fundamental Processes in Mucous and in Ciliated Cells**
  (*K.C. Kim, George Witman* / David Erle / Gunnar Hansson / John Sheehan / Elizabeth Smith / Winfield Sale / Joel Rosenbaum)
- **Genetic Approaches and Mucociliary Diseases**
  (*Heymut Omran, Judith Voynow* / David Schwartz / Michael Knowles / Martina Brueckner)
- **Mucociliary Diseases, Submucosal Glands and Mucus**
  (*Stephen Ballard* / Larry Ostrowski / Michael Welsh / John Engelhardt / Jeff Wine / Ken Adler)
- **Structure-Function Relationships in Cilia and Mucus**
  (*Stephen King, C.W. Davis* / Daniela Nicastro / Richard Cone)
- **Mucociliary and Fluid Interactions**
  (*Michael Rubinstein, Justin Hanes* / Richard Superfine / Carol E. Jones / Chris O'Callaghan / Susan Suarez / Paul Quinton / John Fahy)
- **Life at the Interface: Cilia and Fluid Interactions**
  (*Matthias Salathe* / Hiroshi Hamada / Nicholas LaRusso / Ian Drummond / Stephen King)

COMPUTATIONAL ASPECTS - BIOMOLECULAR NMR

May 22-27, 2011
Il Ciocco Hotel and Resort, Lucca (Barga), Italy
Chair: Stephan Grzesiek
Vice Chair: James H. Prestegard

- **Perspectives for NMR Characterization and Computer Simulation of Biomolecular Behavior**
  (*Stephan Grzesiek* / Lyndon Emsley / Michele Parrinello)
- **New Efficient Experimental and Computational Avenues for Structure Determination**
  (*Lewis Kay* / Alexandre Bonvin / Michele Vendruscolo / David Wishart / Ad Bax)
- **New Experimental Approaches to Detect Biomolecular Dynamics**
  (*Peter Wright* / Hashim Al-Hashimi / Lewis Kay / Art Palmer / Marius Clore / Gabriele Varani)
- **Computer Simulations of Biomolecular Structure and Dynamics**
  (*Martin Blackledge* / Valerie Daggett / David Case / Rafael Bruschweiler)
- **Advances in Speed and Sensitivity of Data Acquisition**
  (*Jeff Hoch* / Lucio Frydman / Guy Montelione)
- **Quantifying Structure and Dynamics of Disordered Protein States**
  (*Rafael Bruschweiler* / Peter Wright / Martin Blackledge / Jane Dyson / Julie Forman-Kay / Markus Zweckstetter)
- **Structure and Dynamics in the Solid State**
  (*Lyndon Emsley* / Mei Hong / Bernd Reif / Rob Tycko)
- **Combining NMR with Complementary Techniques**
  (*Jim Prestegard* / Jill Trewhella / Marcellus Ubbink / Claudio Luchinat)
- **NMR Detection of Biomolecular Function in Complex Systems**
  (*Jane Dyson* / Masahiro Shirakawa / Elaine Holmes)

DENDRITES: MOLECULES, STRUCTURE & FUNCTION

Mar 13-18, 2011
Ventura Beach Marriott, Ventura, CA
Chairs: Erin M. Schuman & Dan Johnston
Vice Chairs: Steven Siegelbaum & Rachel Wong

- **Keynote Presentation: Development of Synaptic Circuits**
  (Josh Sanes)
- **Dendritic Development I**
  (*Rachel Wong* / Deanna Benson / Anirvan Ghosh / Yishi Jin)
- **Dendritic Development II**
  (*Peter Schieffele* / Kim McAllister / Azad Bonni / Kim Tolias / Holly Cline)
- **Dendritic Integration I**
  (*Nelson Spruston* / Jeff Magee / Michael Hausser / Jeff Isaacson)
- **Dendritic Integration II**
  (*Michael Hausser* / Arthur Konnerth / Nace Golding / Peter Jonas / Nelson Spruston)
- **Neuronal Polarity**
  (*Antonella Riccio* / Don Arnold / Bettina Winckler / Frank Polleaux)
- **Dendritic Spines**
  (*Zoltan Nusser* / Kristen Harris / Greg Stuart / Karen Zito / Arthur Konnerth)
- **Connectivity**
  (*Kristen Harris* / Winifred Denk / Mitya Chlovski / Rafa Yuste)
- **Plasticity**
  (*Steve Siegelbaum* / Morgan Sheng / Sam Wang / Arthur Konnerth / Antonella Riccio)
- **Local Processing**
  (*Arthur Konnerth* / Peter Schieffele / Lily Jan)

DENDRITES: MOLECULES, STRUCTURE & FUNCTION (GRS)

Mar 12-13, 2011
Ventura Beach Marriott, Ventura, CA
Chair: Georgeann S. O'Brien
Associate Chair: Denise Cook

The Gordon Research Seminar on Dendrites: Molecules, Structure & Function is a unique forum for graduate students, post-docs, and other scientists with comparable levels of experience and education to present and exchange new data and cutting edge ideas. The goal of this meeting is to encourage social and intellectual interaction among young scientists representing the many facets of dendritic research. Topics will range from cellular dynamics and molecular mechanisms of dendrite development and plasticity to signal integration and processing.

- **Speakers:** To be selected from submitted abstracts
- **Discussion Leaders:** Denise Cook, Megan Corty, Jun Ding, Meron Gurkiewicz, and Neil Schwartz

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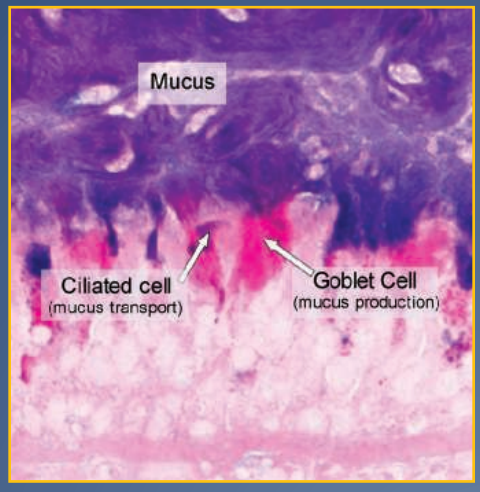

Ciliated cells transport mucus secreted by goblet and glandular cells. Coordinated cilia beating, mucus secretion and ion transport are fundamental life processes and alterations in cilia, mucus, or mucociliary interactions impact numerous diseases. Micrograph: frozen section of a cystic fibrosis lung stained with alcian blue-periodic acid-Schiffs. Image courtesy of Scott H. Randell, University of North Carolina, Chapel Hill. Submitted by Mary C. Rose, Chair, Cilia, Mucus & Mucociliary Interactions GRC.

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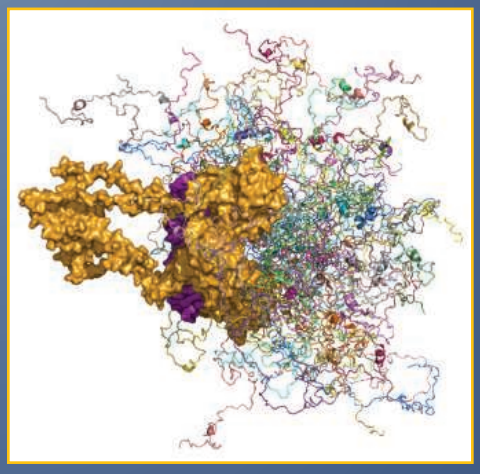

Ensemble structure calculated from combined NMR and SAXS data of the instrinsically unfolded transactivation domain of the tumor suppressor p53 bound to DNA (Wells *et al.* P. Natl. Acad. Sci USA, 2008, vol. 105, 5762-7). *The folded domains are shown in gold and the bound DNA in purple.* Courtesy of Martin Blackledge, Institut de Biologie Structurale Jean-Pierre Ebel, Grenoble, France. Submitted by Stephan Grzesiek, Chair, Computational Aspects of Biomolecular NMR GRC.

FIBRONECTIN, INTEGRINS & RELATED MOLECULES

May 1-6, 2011
Il Ciocco Hotel and Resort, Lucca (Barga), Italy
Chair: David A. Calderwood
Vice Chair: Nick Brown

- **Structure of Integrins and Associated Molecules**
  (Tim Springer / Jun Qin / Tobias Ulmer)
- **Integrin Activation**
  (Mark Ginsberg / Ed Plow / Reinhard Faessler)
- **Signaling through Integrins**
  (Tony Koleske)
- **Adhesion Site Assembly and Dynamics**
  (Ken Yamada / Benny Geiger / Martin Humphries)
- **Cell Migration**
  (Michael Sixt / Peter Friedl / Anna Huttenlocher)
- **Cytoskeletal Dynamics**
  (Dorit Hanein / Frank Gertler / Vic Small)
- **Mechano-Sensing and Mechano-Signaling**
  (Mike Sheetz / Martin Schwartz)
- **Integrins in *In Vivo* and Disease Models**
  (Kairbaan Hodivala-Dilke / Bernhard Nieswandt)
- **Matrix Assembly and Remodeling**
  (Val Weaver / Jean Schwarzbauer / Corinne Albiges-Rizo)

NEW! FIBRONECTIN, INTEGRINS & RELATED MOLECULES (GRS)

Dynamics of Integrin Adhesion and Signaling

Apr 30 - May 1, 2011
Il Ciocco Hotel and Resort, Lucca (Barga), Italy
Chair: Massimiliano Baldassarre
Associate Chair: Benjamin Klapholz

The Gordon-Kenan Research Seminar on Fibronectin, Integrins & Related Molecules is a unique forum for graduate students, post-docs, and other scientists with comparable levels of experience and education to present and exchange new data and cutting edge ideas. This meeting will focus on the dynamics of integrin adhesion and signalling, providing a venue for the attendees to discuss their current research with their peers in the field and to interact with leading scientists from the associated GRC.

- **Speakers:** To be selected from submitted abstracts
- **Discussion Leaders:** Nick Brown and Martin Humphries
- **Keynote Speakers:** Richard Hynes

GASEOUS IONS: STRUCTURES, ENERGETICS & REACTIONS

Feb 27 - Mar 4, 2011
Hotel Galvez, Galveston, TX
Chair: Scott L. Anderson
Vice Chair: Evan R. Williams

- **Spectroscopy of Hydrogen Bonded Clusters**
  (*Mathias Weber* / Daniel Neumark / Anne McCoy)
- **Beam Studies of Ion Chemistry**
  (*Kent Ervin* / Peter Armentrout / Jana Roithova / Mary Rodgers)
- **Conformational Dynamics of Bio-Molecular Ions**
  (*Ryan Julian* / David Clemmer / Albert Heck)
- **Applications to the Real World**
  (*Detlef Schroeder* / Arthur Suits / Emile A. Schweikert / Yu-hui Chiu)
- **Ion Scattering Dynamics**
  (*Karl-Michael Weitzel* / Stefan Willitsch / Jianbo Liu)
- **Electron Attachment and Dissociative Recombination**
  (*Mats Larsson* / Albert Viggiano / Edward Grant / Kristina Hakansson)
- **Spectroscopy and Structure of Metal-Containing Clusters**
  (*Musahid Ahmed* / Michael Duncan / Lai-Sheng Wang)
- **Spectroscopy of Bio-Molecular Ions**
  (*Julia Laskin* / Rebecca Jockusch / Jos Oomens / Lars Andersen)
- **High Field/High Resolution Mass Spectrometry**
  (Alan Marshall)

NEW! GEOBIOLOGY

Jan 30 - Feb 4, 2011
Ventura Beach Marriott, Ventura, CA
Chair: Nora Noffke
Vice Chair: John F. Stolz

- **Early Earth's Physical Evolution**
  (Mark Barley / Yildirim Dilek / Lee Kump)
- **Very Early Life**
  (Chris Fedo / Harold Furnes / Nicola McLoughlin / Steve Mojzsis)
- **Early Sulphur Metabolizing Microbes**
  (Pascal Philipot / Shuhai Xiao / Mark van Zuilen)
- **Early Microbial Mats in Chert and Modern Analogues**
  (Sherry Cady / Jack Farmer / Maud Walsh / Dave Ward)
- **Early Microbial Mats in Sandy Deposits and Modern Analogues**
  (Christoph Heubeck / Nora Noffke / Tony Prave)
- **Banded Iron Formation Biofilms**
  (Andreas Kappler / Kurt Konhauser / Diane Newman)
- **Stromatolites**
  (Kath Grey / David Paterson / Brian Pratt / Pam Reid / Robert Riding / Dawn Sumner)
- **Modern Biofilms**
  (Bill Costerton / Alan Decho / Peter Greenberg / Ron Oremland / Paul Stoodley)
- **Modern Microbial Mats**
  (Jill Banfield / Katrina Edwards / Thomas Neu / Lucas Stal / Pieter Visscher)
- **Archean/Proterozoic Boundary**
  (Alan Jay Kaufman / Martin van Kronendonk)
- **Eukaryotic Life**
  (Stefan Bengtson / Emanuelle Javeaux / Roger Summons / Shucheng Xie)
- **Mars**
  (John Grotzinger)

GLIAL BIOLOGY: FUNCTIONAL INTERACTIONS AMONG GLIA & NEURONS

Mar 6-11, 2011
Four Points Sheraton / Holiday Inn Express
Ventura, CA
Chair: Philip G. Haydon
Vice Chair: Brian A. Macvicar

- **Astrocytic Modulation of Synaptic Plasticity**
  (Stephane Oliet / Andrea Volterra / Jaideep Bains / Ken McCarthy)
- **Behavioral and Circuit Roles for Astrocytes**
  (Pierre Magistretti / Hajime Hirase / Tommaso Fellin / Frank Kirchoff)
- **Roles for Glia in Disorders of the Nervous System**
  (Jeff Rothstein / Mike Salter)
- **Roles of Microglia in Disorders of the Brain**
  (Joe El Khoury / Harald Neumann / Marco Prinz / Richard Ransohoff)
- **Functions of Glial Connexins and Pannexins**
  (Steve Scherer / David Spray / Christian Giaume)
- **Synapse-Glial Interactions**
  (Bal Khakh / Dwight Bergles / David Attwell / Alfonso Araque)
- **Control of the Vasculature by Glial Cells**
  (Eric Newman / Brian MacVicar / Serge Charpak)
- **Roles of Glia in Synapse Development**
  (Ben Barres / Beth Stevens / Angelique Bordey)
- **Epilepsy and Glia**
  (Douglas Coulter / Giorgio Carmignoto / Detlev Boison)

GLYCOBIOLOGY

May 8-13, 2011
Il Ciocco Hotel and Resort, Lucca (Barga), Italy
Chair: Hudson H. Freeze
Vice Chair: Kelley W. Moremen

- **Keynote Presentation: Translating the Third Language of Life**
  (Lawrence Tabak)
- **Glycans in Metabolism and Signaling**
  (*Gerald Hart* / James Dennis / Richard Cummings / Dona Love)
- **Immunology and Immune Response**
  (*James Paulson* / Robert Sackstein / Jeffrey Ravetch / Teunis Geijtenbeek)
- **Microbes and Parasites**
  (*Richard Cummings* / Irma van Die / Markus Aebi / Adam Godzik)
- **Developmental Glycobiology**
  (*Pamela Stanley* / Kelly Ten Hagen / Hannes Buelow / Robert Haltiwanger)
- **Glycan Structure and Recognition**
  (*Ronald Schnaar* / Kurt Drickamer / Rob Woods / Fred Brewer / William Balch)
- **Glycosylation Disorders and Therapy**
  (*Thierry Hennet* / Yu Yamaguchi / Ronald Schnaar)
- **Glycans in Physiology**
  (*Jeffrey Esko* / Jacques Baenziger / Ajit Varki)
- **Glycans in Cancer**
  (*James Dennis* / Hisashi Narimatsu / Frederic Bard)

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- **Glycan Engineering and Stem Cells**
  (*Robert Sackstein* / Mike Tiemeyer / Catherine Merry / James Paulson / Lai-Xi Wang / Jamey Marth)
- **Glycomics and GlycoChemistry**
  (*Anne Dell* / David Vocadlo / Linda Hsieh-Wilson / Rob Field)

NEW! IMMUNOLOGY OF FUNGAL INFECTIONS
Jan 16-21, 2011
Hotel Galvez, Galveston, TX
Chair: Gordon Brown
Vice Chairs: Stuart M. Levitz & Luigina Romani

- **Fungal PAMPS**
  (*Daniel Poulain* / Frans Klis / Neil Gow / William Goldman)
- **Innate Fungal Recognition**
  (*Carl Figdor* / Mihai Netea / Joseph El Khoury / Jurgen Ruland)
- **Adaptive Immunity and Immune Regulation**
  (*Anna Vecchiarelli* / Caetano Reis e Sousa / Arturo Casadevall)
- **Organ-Specific Immunity**
  (*Francoise Dromer* / Cory Hogaboam / Paul Fidel / Bernhard Hube)
- **Fungal Diseases and Immunodeficiency**
  (*David Denning* / Kieren Marr / Brahm Segal)
- **Immunity to Specific Pathogens**
  (*Bruce Klein* / Vera Calich / Frank Ebel / Chad Steele)
- **Immunotherapy and Vaccination**
  (*Scott Filler* / Tom Walsh / Antonio Cassone)
- **Fungal Diseases as a Consequence of Immunomodulation**
  (*Jay Kolls* / Nina Singh / George Deepe / Kazuyoshi Kawakami / Flavia De Bernardis)
- **From Bench to Bedside and Back Again**
  (*Bart Jan Kullberg* / Liise-anne Pirofski / Tom Harrison)

In vivo two-photon image of P22 mouse cortex. Portion of an apical tuft from a layer 2/3 pyramidal cell that was labeled with EGFP using in utero electroporation. Courtesy of Alberto Cruz-Martín (Carlos Portera-Cailliau lab), UCLA. Submitted by Georgeann S. O'Brien, Chair, Dendrites: Molecules, Structure & Function GRS.

INORGANIC REACTION MECHANISMS
Mar 6-11, 2011
Hotel Galvez, Galveston, TX
Chair: Seth N. Brown
Vice Chair: Mahdi M. Abu-Omar

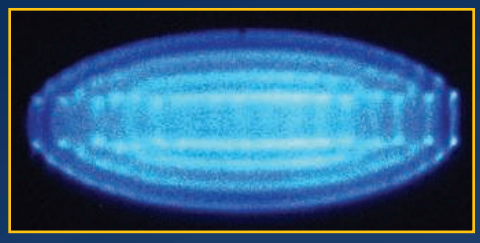
- **Small Molecule Activation**
  (*Jim Mayer* / Dan Mindiola / David Milstein)
- **Atom and Electron Transfer**
  (*Carol Creutz* / Leif Hammarström / Sharon Hammes-Schiffer / Tai-Chu Lau / Jeremy Smith)
- **Redox Catalysis**
  (*Jonas Peters* / Alan Heyduk / Shannon Stahl)
- **Bioinorganic**
  (*Patrick Holland* / Dan Stack / Jennifer DuBois / Marcetta Darensbourg / Marty Bollinger)
- **Polymerization**
  (*John Walzer* / Jerzy Klosin / Geoff Coates)
- **O_2 Activation and Formation**
  (*Klaus Theopold* / Jake Soper / Antoni Llobet / Andreja Bakac / Jim Muckerman)
- **Applications in Organic Synthesis**
  (*Laurel Schafer* / Vy Dong / Shane Krska)
- **Organometallics**
  (*Oleg Ozerov* / Andrei Vedernikov / Odile Eisenstein / Jackie Kiplinger / Doug Grotjahn)
- **Olefin Metathesis**
  (*Jack Norton* / Robert Grubbs)

INSULIN-LIKE GROWTH FACTORS IN PHYSIOLOGY & DISEASE
Feb 27 - Mar 4, 2011
Ventura Beach Marriott, Ventura, CA
Chair: Rosemary O'Connor
Vice Chair: Robert Smith

- **Stress Responses, Energy and Ageing**
  (Claire Bastie / Valter Longo)
- **Somatic Growth, and Regeneration**
  (Maria Grant / Peter Rotwein)
- **Signalling Pathways and Regulation**
  (Davide Ruggero / Olle Larsson / Linda Schuler)
- **IGFs Binding Proteins**
  (Leon Bach / Cheryl Conover)
- **Cancer**
  (Pnina Brodt / Dale Ludwig / Brendan Manning)
- **Regulation of Ligand / Receptor Function**
  (Antonino Belfiore)
- **Neurogenesis and Neurodegeneration**
  (Friedrick Metzger / Andrew Dillin / Derek Van der Kooy)
- **Modulating IGF Actions: Issues for the Future**

NEW! LYSOSOMAL DISEASES
Jan 23-28, 2011
Hotel Galvez, Galveston, TX
Chair: Tony Futerman
Vice Chair: Frances Platt

- **History and Current Status**
  (*Tony Futerman, Fran Platt* / Tim Cox / Liz Neufeld)
- **Basic Lysosomal Biology**
  (*Fred Maxfield, Paul Pryor* / Paul Luzio / Antony Galione / Juan Bonifacino)
- **Relationships to Other Diseases**
  (*Raffi Schiffmann, John Hardy* / Ellen Sidransky / Ralph Nixon)
- **Pathogenic Cascades**
  (*Steve Walkley, Ed Schuchman* / Jon Cooper / Andrea Ballabio / Sandra D'Azzo)
- **Biomarkers**
  (*John Hopwood, Cynthia Tift* / Dan Ory / Hans Aerts)
- **Defective Lysosomal Transmembrane Proteins**
  (*Bruno Gasnier, Thomas Braulke* / Susan Slaugenhaupt / Yannis Ioannou / Sue Cotman)
- **Experimental Therapies**
  (*Roscoe Brady, Bill Sly* / Jean Michel Heard / Bev Davidson / Don Mahuran)
- **Poster Presentations and Hot Topics**
  (*Maurizio Scarpa, Emyr Lloyd Evans, Thierry Levade, Volkmar Gieselman, Marie Vanier*)
- **Clinical Trial Design and Outcomes**
  (*Marc Patterson, Greg Pastores* / Ed Kaye / Denny Porter)



Fluorescence image of a Coulomb crystal of laser-cooled Ca^+ ions in an ion trap containing 26 sympathetically cooled, rotationally state-selected N^{2+} ions in the center for use in ultracold ion-molecule collision and reaction experiments. Courtesy of Stefan Willitsch, University of Basel, Switzerland. Submitted by Scott L. Anderson, Chair, Gaseous Ions: Structures, Energetics & Reactions GRC.

MACROMOLECULAR MATERIALS
Jan 9-14, 2011
Four Points Sheraton / Holiday Inn Express
Ventura, CA
Chair: Todd S. Emrick
Vice Chair: Alfred J. Crosby

- **Patterning and Directed Assembly: From Nano to Meso-Materials**
  (Chad Mirkin / Anna Balazs)
- **Solution Assembly of Macromolecules and Functional Polymer Chemistry**
  (Guiseppe Battaglia / Darrin Pochan / Craig Hawker)
- **Interfacial Interactions in Macromolecular Systems**
  (Kari Dalnoki-Veress / Andreas Fery)
- **The Polymer-Biology Interface: Assembly and Delivery**
  (David Lynn / Jianjun Cheng / Mark Grinstaff / Yao Lin)
- **Polymers and Nanocomposites: From Dispersed to Highly Ordered Structures**
  (Tom Russell / Richard Vaia)
- **Conjugated Organic and Macromolecular Materials: Synthesis and Devices**
  (Alex Jen / Frieder Jaekle)
- **Bio-mimetic Materials and *In Vivo* Applications**
  (Molly Shoichet / Ting Xu)
- **Novel Macromolecules: From Synthesis to Applications**
  (Chris Bielawski / James Hedrick / Marc Hillmyer)
- **Polyelectrolytes, Gels, and Self-Assembled Systems**
  (Jian Ping Gong / Ryan Hayward)

MACROMOLECULAR MATERIALS (GRS)
Macromolecular Innovation for Sustainability and Materials Performance
Jan 8-9, 2011
Four Points Sheraton / Holiday Inn Express
Ventura, CA
Chair: Samantha McRae
Associate Chair: Michael Bartlett

The Gordon Research Seminar on Macromolecular Materials (GRS) is a unique forum for graduate students, post-docs, and other scientists with comparable levels of experience and education to present and exchange new data and cutting edge ideas. The aim of the Seminar is to provide an interdisciplinary program solely for younger researchers, connecting the synthetic, physical, chemical and biological aspects of macromolecules. The intimate and interdisciplinary nature of the Macromolecular Materials GRS guarantees a memorable meeting that will enrich the

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future scientific endeavors of its participants.

- **Speakers:** To be selected from submitted abstracts
- **Discussion Leaders:** To be selected from submitted abstracts

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MAMMALIAN DNA REPAIR

Feb 6-11, 2011
Four Points Sheraton / Holiday Inn Express
Ventura, CA
Chair: Leona D. Samson
Vice Chair: Tanya T. Paull

- **Keynote Presentations**
  (*Leona Samson* / Lorena Beese / Penelope Jeggo)
- **Structural Biology of DNA Repair**
  (*Priscilla Cooper* / Samuel Wilson / John Tainer / Jacqueline Barton / Priscilla Cooper / Tom Ellenberger)
- **DNA Damage Signaling**
  (*Tanya Paull* / Yosef Shiloh / Tanya Paull / William Dunphy / David Cortez)
- **Recombination & Genome Stability**
  (*Bevin Engelward* / Bevin Engelward / Andre Nussenzweig / Orlando Scharer / Susan Lees-Miller)
- **Base Lesion Repair**
  (*Eugenia Dogliotti* / Primo Schar / Arne Klungland / Joann Sweasy / Eugenia Dogliotti)
- **DNA Repair in the Context of Chromatin**
  (*Jessica Downs* / Genevieve Almouzni / Jessica Tyler / Michael Smerdon / Leon Mullenders / Jessica Downs)
- **DNA Repair and Neurodegeneration**
  (*Keith Caldecott* / Keith Caldecott / Peter McKinnon / Martin Lavin)
- **DNA Repair, Human Disease & Aging**
  (*Laura Niedernhofer* / William Copeland / Wim Vermeulen / Laura Niedernhofer / Michael Lieber)
- **Systems-Wide Responses to DNA Damage**
  Trey Ideker / Trey Ideker / Thomas Begley / Mark O'Connor)

This dome-shaped structure is preserved in the about 3 billion years old Pongola sandstone, South Africa. The gas was accumulating beneath a microbial mat. This microbial mat was fossilized in situ. Height of dome about 15 cm. Submitted by Nora Noffke, Chair, Geobiology GRC.

METALS IN BIOLOGY

Jan 30 - Feb 4, 2011
Four Points Sheraton / Holiday Inn Express
Ventura, CA
Chair: William B. Tolman
Vice Chair: Michael J. Maroney

- **Bioinorganic Approaches Toward Interconverting Protons, Electrons, and Dihydrogen**
  (*Harry Gray* / Wolfgang Lubitz / Fraser Armstrong)
- **Bioinorganic-Inspired Energy Science**
  (*Vince Pecoraro* / Gary Brudvig / David Britt / John Golbeck / Joan Broderick)
- **Sensors and Medicine: From Metalloneurochemistry to Alzheimers**
  (*Christopher Chang* / Shawn Burdette / Amy Palmer / Caryn Outten)
- **Multiple Electron Redox Catalysis in Metallobiochemistry**
  (*Marcetta Darensbourg* / Jonas Peters / Thomas Rauchfuss / Joel Weiner / Marty Kirk)
- **Biocatalyst Construction: Metallocenter Assembly and Cofactor Biogenesis**
  (*Squire Booker* / Carrie Wilmot / Akif Tezcan / Michael Maroney)
- **Metals and DNA / RNA**
  (*Jackie Barton* / Victoria DeRose / Nicholas Farrell / Eugen Stulz / Ulrich Bierbach)
- **Environmental Bioinorganic Chemistry**
  (*Peter Kroneck* / Elisabeth Bouwman / Daniel Dubois / Paul Falkowski)
- **From Synthetic Models to Biocatalysis: Selective Oxidations**
  (*Rachel Austin* / Olivia Reinaud / Sonya Franklin / Lawrence Que, Jr. / Michael Green)
- **Joint Session with Bioinorganic Chemistry GRS**
  (*Ann Walker* / Alison Butler)

BIOINORGANIC CHEMISTRY (GRS)

Feb 3-6, 2011
Four Points Sheraton / Holiday Inn Express
Ventura, CA
Chair: Christine M. Phillips
Vice Chair: Robert J. Radford

The Gordon Research Seminar on Bioinorganic Chemistry is a unique forum for graduate students, post-docs, and other scientists with comparable levels of experience and education to present and exchange new data and cutting edge ideas. Speakers will be selected from submitted abstracts. Session topics and Discussion Leaders are listed below:

- **Joint Session with Metals in Biology GRC followed by GRS Poster Session**
- **Metals in Extreme Environments**
  (*Ann Valentine*)
- **Bioinorganic Methods and Technique Development**
  (*Sean Elliott*)
- **Modeling and Characterizing Metalloenzyme Active Sites**
  (*Andy Borovik*)
- **Metal Homeostasis in the Cell and Environment**
  (*John Magyar*)
- **Metal Clusters and Cofactors in Biology**
  (*Sonya Franklin*)

MOLECULAR PHARMACOLOGY

Jan 9-14, 2011
Ventura Beach Marriott, Ventura, CA
Chair: Paul Insel
Vice Chairs: Jean-Philippe Pin & Brigitte Kieffer

- **Receptor Structure: What it Says About Function**
  (*Jean-Phillipe Pin* / Brian Kobilka / Ray Stevens)
- **Novel Methods and New Insights Regarding GPCR Signaling**
  (*Brigitte Kieffer* / Arthur Christopoulos)
- **Cellular Organization of Receptors and Signaling Proteins: Molecular and Functional Microdomains I**
  (*Mark Rasenick* / Hemal Patel)
- **Signaling via G-proteins: What's Old is New**
  (Roger Sunahara / Alan Smrcka)
- **Cellular Organization of Receptors and Signaling Proteins: Molecular and Functional Microdomains II**
  (*Susanna Cotecchia* / JoAnn Trejo)
- **Disease-Related Changes in Receptor Signaling: Therapeutic Implications**
  (*Joel Bockaert*)
- **New Drugs Derived from New Ideas and New Findings**
- **Animal Models of GPCRs in Disease**
  (*Mark von Zastrow*)

NEW! MOLECULAR PHARMACOLOGY (GRS)

Jan 8-9, 2011
Ventura Beach Marriott, Ventura, CA
Chair: Aaron Snead
Associate Chair: Michael P. Bokoch

The Gordon-Kenan Research Seminar on Molecular Pharmacology is a unique forum for graduate students, post-docs, and other scientists with comparable levels of experience and education to present and exchange new data and cutting edge ideas. The focus of this meeting is to engage young scientists and trainees in discussion of 3 aspects of G Protein-Coupled Receptors (GPCRs) and post-receptor components: 1) Structural biology, 2) Cell biology and 3) Physiological roles. These 3 aspects largely subsume recent and current work in the field and thus should provide participants with state-of-the-art knowledge prior to the associated GRC.

- **Speakers:** To be selected from submitted abstracts
- **Discussion Leaders:** Susanna Cotecchia, JoAnn Trejo, and Mark von Zastrow. Student discussion leaders will be selected from submitted abstracts.
- **Keynote Speakers:** Brian Kobilka

NITRIC OXIDE

Understanding the Biology and Chemistry of Its Formation, Action and Signaling

Feb 13-18, 2011
Four Points Sheraton / Holiday Inn Express
Ventura, CA
Chair: Martin Feelisch
Vice Chair: Jon Lundberg

- **Making NO - Comparing the Bacterial, Plant and Mammalian Toolkit**
  (*William C. Sessa* / Brian R. Crane / Werner M. Kaiser / Dennis Stuehr)
- **Chemical Biology: Storage, Transport and Nitrogen Oxide Cycling**
  (*Jay Zweier* / Jack Lancaster / Jon O. Lundberg / Richard Weller)

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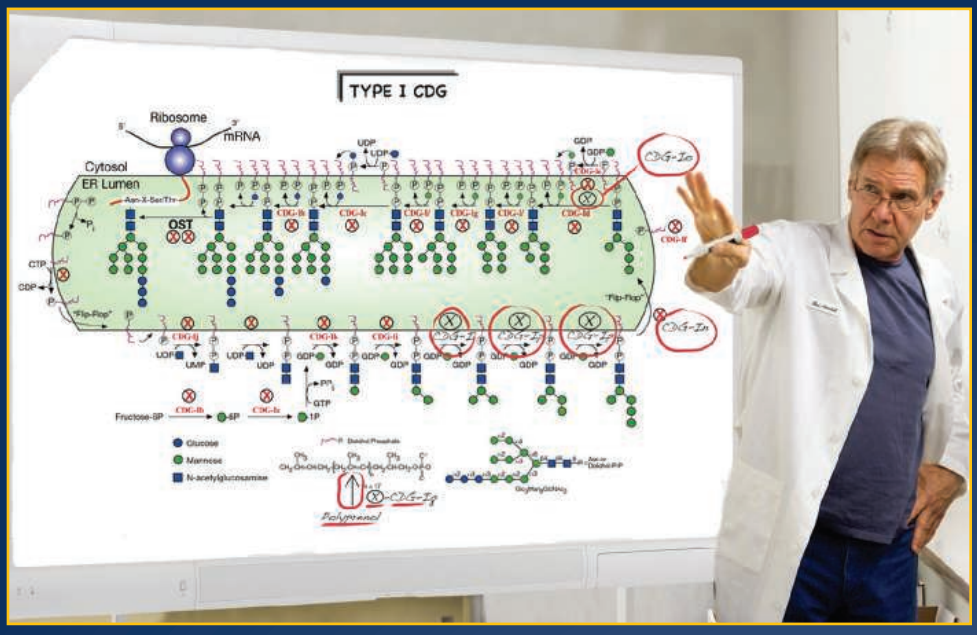
- **NO-cGMP Signal Transduction**
  (*John Garthwaite* / William R. Montfort / Doris Koessling / Harald HHW Schmidt / Takaaki Akaike)
- **Thiol/Redox Signaling and Nitration - Regulation and Significance**
  (*William R. Montfort* / Jonathan S. Stamler / Michael Murphy / Harry Ischiropolous)
- **Coping with Oxygen Shortage - HIF, Mitochondria and Altitude Physiology**
  (*Serpil Erzurum* / Bernhard Bruene / Paul T. Schumacker / Michael Grocott / Cynthia M. Beall)
- **Substrate Utilization, Intermediary Metabolism and Mechanisms of Resistance**
  (*Andrew Gow* / Thomas Hintze / Carl Nathan / Joerg Durner / Dean P. Jones)
- **Current Controversies and Late Breaking Findings / Hot Topics**
  (*Victor Darley-Usmar, Mark T. Gladwin*)
- **From Bedside to Bench and Back - What's New on the Therapeutic Horizon?**
  (*Malte Kelm* / Eddie Weitzberg / Amrita Ahluwalia / Paola Tochetti / Warren M. Zapol)
- **NO-Heme Interactions and Nitroxyl**
  (*Peter Ford* / David Wink / George Richter-Addo / S. Bruce King)



"Extraordinary Measures" star Harrison Ford circles newly discovered Congenital Disorders of Glycosylation. Participants at the Glycobiology GRC will hear much more about these disorders when they come to Italy. Image adapted by Doug Haynes from the film "Extraordinary Measures" with permission of Harrison Ford and from *Essentials of Glycobiology* Second Edition with permission of the Consortium of Glycobiology Editors. Submitted by Hudson Freeze, Chair, Glycobiology GRC.

OXIDATIVE STRESS & DISEASE

Emerging Research Areas in the Study of Oxidative Stress and Disease

Mar 13-18, 2011
Four Points Sheraton / Holiday Inn Express
Ventura, CA
Chairs: Julie K. Andersen & Michael Brownlee
Vice Chairs: Tilman Grune & Enrique Cadenas

- **Keynote Presentation: Oxidative Stress and Cellular Dysfunction: Examples from Neurodegenerative Disease**
  (Flint Beal)
- **Oxidative Stress, DNA Damage, Epigenetics, and Disease**
  (*Jan Vijg, Judy Campisi* / Jan Vijg / Judy Campisi / Goeff Rosenfeld)
- **Oxidative Stress and Transcriptional Regulation in Disease**
  (*Henry Forman* / Raj Ratan / Noel Buckley / King Jordon)
- **Oxidative Stress, miRNAs, and Disease**
  (*Myriam Goropse* / Myriam Goropse / Marai Mouradian)
- **Oxidative Stress, Stem Cells, and Disease**
  (*Victoria Lunyak* / Victoria Lunyak / Tom Rando / David Scanden)
- **Oxidative Stress and Alterations in Mitochondrial Dynamics in Disease**
  (*Tim Greenamyre* / Teresa Hastings / Charleen Chu / John Le Masters)
- **Complications in Diabetes and Oxidative Stress**
  (*Angelika Bierhaus* / Sam El-Osta / Geoffrey Gurtner / Erwin Bottinger)
- **Inflammation, Oxidative Stress, and Cardiovascular Disease**
  (*Joseph Witztum* / Ming-Hui Zou / Jean Schaffer / Philipp Scherer)
- **Short Presentations from Posters / Late-Breaking Advances**
  (*Julie Andersen / Michael Brownlee*)

NEW! OXIDATIVE STRESS & DISEASE (GRS)

Common "Threads" in Oxidative Stress-Mediated Diseases

Mar 12-13, 2011
Four Points Sheraton / Holiday Inn Express
Ventura, CA
Chair: Almas Siddiqui
Associate Chair: Aric Rogers

The Gordon-Kenan Research Seminar on Oxidative Stress & Disease is a unique forum for graduate students, post-docs, and other scientists with comparable levels of experience and education to present and exchange new data and cutting edge ideas. The focus of this meeting is to expose an outstanding and diverse group of young investigators to major underlying mechanistic themes and cutting-edge technologies in the field of oxidative stress and disease. A career orientation session led by Dr. Cathryn Kunst will cover the following topics: 1. Opportunities and challenges in academic versus industrial research; 2. Successful research fundraising; 3. Principles in lab mentorship; and 4. Successful networking.

- **Speakers:** To be selected from submitted abstracts
- **Discussion Leaders:** Julie Andersen, Tom Prolla, and Victoria Lunyak
- **Mentorship Component:** Career panel, led by Cathryn Kunst

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NEW! PHYSICAL VIROLOGY

Jan 16-21, 2011
Ventura Beach Marriott, Ventura, CA
Chair: Bogdan Dragnea
Vice Chairs: Peter E. Prevelige & M.G. Finn

- **Structure**
  (*Elizabeth R. Wright* / Wah Chiu / J.A.G. Briggs)
- ***In Singulo* Virology**
  (*Rob Phillips* / Alex McPherson / Itay Russo / Urs Greber)
- **Mechanisms of Self-Assembly**
  (*Carolyn Teschke* / Adam Zlotnick / William Gelbart)
- **Theoretical Models for Regular Structures and Their Assembly**
  (*Roya Zandi* / Klaus Schulten / Dennis Rapaport / Charles L. Brooks III)
- **Viruses as Dynamic Systems**
  (*Jack Johnson* / Alex Evilevitch / Albert Heck)
- **Virus-Based Materials**
  (*Trevor Douglas* / Qian Wang / Takafumi Ueno / Dale Evans)
- **Biomedical Applications**
  (*Nicole Steinmetz* / Suchetana Mukhopadhyay / Peter Stockley)
- **Connecting Multiple Scales**
  (*Jim deYoreo* / Bertrand Garcia-Moreno / Vicky Colvin / David Holcman)
- **Late-Breaking Topics**
  (Abraham (Avi) Minski / Alan Rein)

NEW! PHYSICAL VIROLOGY (GRS)

Jan 15-16, 2011
Ventura Beach Marriott, Ventura, CA
Chair: Stella E. Aniagyei

The Gordon-Kenan Research Seminar on Physical Virology is a unique forum for graduate students, post-docs, and other scientists with comparable levels of experience and education to present and exchange new data and cutting edge ideas. The focus of this meeting is on: 1. providing a non-intimidating forum for the discussion of physical, biological, and materials perspectives that are rapidly shaping the field of viruses as physical functional systems; and 2. providing career mentorship by addressing the challenges and opportunities related to interdisciplinary research, including: how to create one's niche in a diverse field, what types of jobs are available to applicants with an interdisciplinary background, and how the continuous evolution of this field might impact future career prospects.

- **Speakers:** To be selected from submitted abstracts

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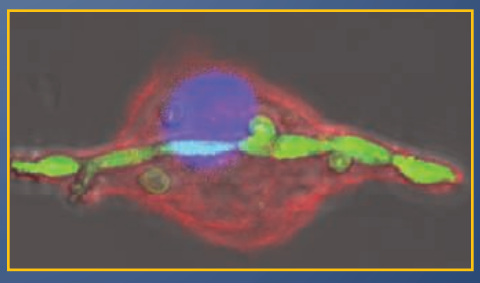
- **Discussion Leaders:** Walid Maaty, Antonette Bennett, and Hazel Levy
- **Keynote Speakers:** Mavis Agbandje-McKenna
- **Mentorship Component:** "Challenges and Opportunity in Interdisciplinary Research", a career panel featuring Nicole Steinmetz , Joseph C.Y. Wang, Kelly Lee and Junghae Suh



Confocal image showing a thioglycollate elicited macrophage (red) following ingestion of Fonsecaea pedrosoi hyphae (green). The host cell nucleus is stained in blue. Courtesy of Gloria Sousa and Gordon Brown, University of Aberdeen. Submitted by Gordon D. Brown, Chair, Immunology of Fungal Infections GRC.

NEW! PLANT LIPIDS: STRUCTURE, METABOLISM & FUNCTION
Jan 30 - Feb 4, 2011
Hotel Galvez, Galveston, TX
Chairs: Christoph Benning & Jan Jaworski
Vice Chairs: Ruth Welti & Edgar Cahoon

- **Lipid Adaptations in Response to a Changing Environment**
  (*Peter Doermann* / Benjamin van Mooy / Hiroyuki Ohta)
- **Lipids Involved in Endomembrane and Plasma Membrane Structure and Function**
  (*Edgar Cahoon* / Sebastien Mongrand / Mee-Len Chye)
- **Lipids in Protection of Plants against Abiotic and Biotic Stresses**
  (*Ljerka Kunst* / Asaph Aharoni / Owen Rowland)
- **Lipid Signaling in Plant Development and Homeostasis**
  (*Sam Wang* / Glenda Gillaspy / Kent Chapman)
- **Lipid Molecules as Building Blocks for the Assembly of the Photosynthetic Membrane**
  (*Hiroyuki Ohta* / Gilles Basset / Rebecca Roston)
- **Lipid Droplet and Lipid Body Formation, Maintenance, and Turnover**
  (*Ivo Feussner* / Robert V. Farese, Jr. / Quiang Hu)
- **Analysis of Triacylglycerols and other Lipids**
  (*Ruth Welti* / Tony Larson / Jonathan Markham)
- **Lipids and Fatty Acids for Human Health and Industrial Purposes**
  (*Anthony Kinney* / Edgar Cahoon / Joerg Bauer)
- **Regulation of Plant Lipid Metabolism: A Target for Engineering**
  (*Jan Jaworski* / Doug Allen / Jay Thelen)

POLAR MARINE SCIENCE
Exploring Complex Systems in Polar Marine Science
Mar 20-25, 2011
Four Points Sheraton / Holiday Inn Express
Ventura, CA
Chair: Patricia L. Yager
Vice Chair: Christine Michel

- **Keynote Presentation: Polar System Complexity and Climate Change**
  (*Patricia Yager* / Doug Capone)
- **Polar Atmospheric Circulation, Sea Ice, and Climate**
  (*Cathleen Geiger* / Marilyn Raphael / Mark Serreze / Daniel Feltham / Don Perovich)
- **Ocean Mixing, Circulation, and Links to Global Climate**
  (*Luc Rainville* / Susan Lozier / Rebecca Woodgate)
- **Biogeochemical Complexity in Ice and Seawater**
  (*Roxanne Maranger* / Jean-Louis Tisson / Victoria Fabry)
- **Methane Hydrates: Nonlinear Links Between Carbon and Climate**
  (*Laura Lapham* / Charlie Paull)
- **Carbon Fluxes and the Biological Pump as Integrators of Complexity?**
  (*Adrian Burd* / Paul Wassman)
- **Genomic and Proteomic Illustrations of Microbial Biocomplexity**
  (*Laura Alonso Saez* / Carlos Pedros Alio / Mak Saito)
- **Do Higher Tropic Levels Integrate or Add Complexity?**
  (*Paul Renaud* / Craig Smith / Jaume Forcada)
- **Moving Forward from Here: Improving our Observations of Polar Complexity**
  (*Marcel Babin* / Oscar Schofield)

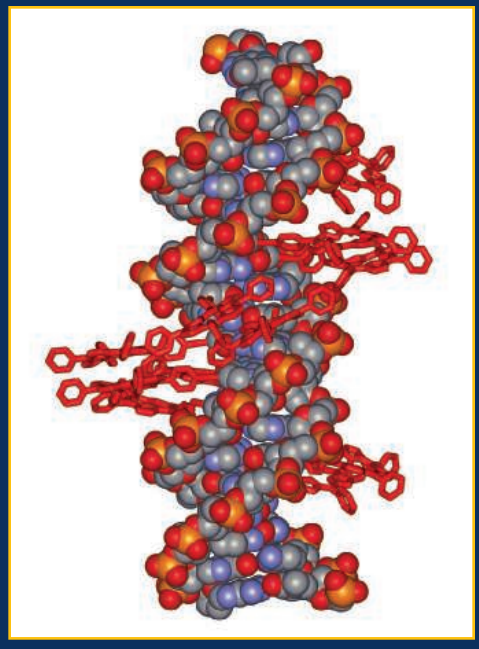
NEW! POLAR MARINE SCIENCE (GRS)
Contributing to the Understanding of Complex Polar Marine Systems
Mar 19-20, 2011
Four Points Sheraton / Holiday Inn Express
Ventura, CA
Chair: Penelope M. Wagner
Vice Chair: Christine Michel

The Gordon-Kenan Research Seminar on Polar Marine Science is a unique forum for graduate students, post-docs, and other scientists with comparable levels of experience and education to present and exchange new data and cutting edge ideas. The focus of this meeting will be exploring the contribution of graduate research to understanding the complex systems that make up polar marine science. Knowledge of how these systems interact and making future predictions requires a multifaceted approach that incorporates both biological and physical sciences. The interdisciplinary nature of this topics calls for research that focuses on interactions among components. This GRS forum will provide the opportunity for students to present their work and understand how it contributes to understanding the polar marine science system as a whole, as well as to discuss how individual science can contribute to this challenge.

- **Speakers:** To be selected from submitted abstracts
- **Discussion Leaders:** Cameron McNaughton and Gina Henderson
- **Keynote Speakers:** Pat Langhorne and Paul Wassmann

QUANTITATIVE GENETICS & GENOMICS
From Genome to Phenotype
Feb 20-25, 2011
Hotel Galvez, Galveston, TX
Chair: Peter M. Visscher
Vice Chair: Jack Dekkers

- **Quantitative Genetics is Alive and Kicking**
  (*Peter Visscher* / Bill Hill / Jonathan Flint)
- **Next Generation Genetics**
  (*Manolis Dermitzakis* / Deborah Nickerson)
- **Systems Genetics to Unravel Phenotypic Variation**
  (*Greg Gibson* / Charles Boone / Stephen Montgomery)
- **Has the Era of Molecular Breeding (Finally) Arrived?**
  (*Dorian Garrick* / Ben Hayes / Geoff Graham)
- **Quantitative Genomics of Adaptation**
  (*Matt Keller* / Carlos Bustamante / Kerstin Lindblad-Toh / Anna Di Rienzo)
- **Statistical Genetics and Genomics**
  (*Jack Dekkers* / Gil McVean / Dan Nettleton)
- **Evolutionary Quantitative Genetics and Genomics**
  (Margaret Mackinnon / Jeffrey Barrick)
- **The Power of Sequenced Resource Populations to Map Trait Loci**
  (*Mike Goddard* / Goncalo Abecasis / Gary Churchill)
- **From Association to Function**
  (Michel Georges / Antoni Rafalski)



The calculated structure of an eleven porphyrin-DNA zipper array, which reversibly forms a photonic wire upon hybridisation of the DNA. Courtesy of Eugen Stulz (University of Southhampton), Speaker, Metals in Biology GRC. Submitted by William B. Tolman, Chair, Metals in Biology GRC.

NEW! RENEWABLE ENERGY: SOLAR FUELS
Jan 16-21, 2011
Four Points Sheraton / Holiday Inn Express
Ventura, CA
Chairs: Leif Hammarstrom & Joseph T. Hupp
Vice Chairs: Wolfgang Lubitz & Thomas Mallouk

- **Photosynthesis and Hybrid Systems**
  (Junko Yano / Victor Batista / Mattias Rögner)
- **Fuel Producing Enzymes**
  (Fraser Armstrong / Holger Dobbek)
- **Microorganisms for Direct Solar Fuel Production**
  (Olaf Kruse / Anastasios Melis)
- **Heterogeneous Systems for Solar Fuels Production I**
  (Nate Lewis / Andrew Peterson / Frank Osterloh)
- **Heterogeneous Systems for Solar Fuels Production II**
  (Craig A Grimes / Yogesh Surendranath / Kevin Sivula)
- **Molecular Catalysis for CO_2 Reduction and H_2 Formation I**
  (Dan Dubois/ Jeffrey R. Long / Marcetta Darensbourg)

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- **Molecular Catalysis for CO_2 Reduction and H_2 Formation II**
  (Vincent Artero / Sascha Ott / Andrew Bocarsly / Mei Wang)
- **Molecular Catalysts for Water Splitting**
  (Javier Concepcion / Toni Llobet / Craig Hill)
- **Solar Fuels: Outlook and New Ideas**
  (*Tom Mallouk, Wolfgang Lubitz* / Athanasios G. Konstandopoulos / Sossina Haile)

RENEWABLE ENERGY: SOLAR FUELS (GRS)

Jan 15-16, 2011
Four Points Sheraton / Holiday Inn Express
Ventura, CA
Chair: Clyde W. Cady
Associate Chair: Alex B.F. Martinson

The Gordon Research Seminar on Renewable Energy: Solar Fuels is a unique forum for graduate students, post-docs, and other scientists with comparable levels of experience and education to present and exchange new data and cutting edge ideas. The Renewable Energy: Solar Fuels GRS will examine the science that underlies solar fuels production including light capture, charge separation and multi-electron catalysis. The meeting will bring together a diverse group of young researchers studying the relevant materials, molecular systems, and biological/bio-mimetic assemblies.

- **Speakers:** To be selected from submitted abstracts
- **Discussion Leaders:** Leif Hammarström, Joseph Hupp
- **Keynote Speakers:** Marc Fontecave

RNA EDITING
Editing and Modification of RNA and DNA

Jan 9-14, 2011
Hotel Galvez, Galveston, TX
Chairs: Eric Phizicky & Kazuko Nishikura
Vice Chairs: Robert Reenan & Nina Papavasiliou

- **Evolution and Diversity in Editing and Modification**
  (*Janusz Bujnicki* / Eli Eisenberg / Henri Grosjean / Tsutomu Suzuki)
- **Target Site Recognition and Catalysis by Editing and Modification Enzymes**
  (*Jane Jackman* / Nina Papavasiliou / Stefan Maas / Juan Alfonzo / Jonatha Gott)
- **Editing and Innate Immunity**
  (*Reuben Harris* / Tasuko Honjo / Charles Samuel)
- **Regulation of Editing and Modification**
  (*Marie Öhman* / Gloria Culver / Maureen Hanson / Pal Falnes / Pat Limbach)
- **Editing, Viral Infection and Host Defense**
  (*Michael Malim* / Harold Smith / Joseph Wedekind)
- **Macromolecular Machines and Functional Interactions**
  (*Ken Stuart* / Larry Simpson / Yi-Tao Yu / Tom Meier / Jorge Cruz-Reyes)
- **Structural Insights into RNA Editing and Modification**
  (*Hong Li* / Raven Huang / Osamu Nureki)
- **Biological and Medical Impact of Editing and Modification**
  (*Ron Emeson* / Anders Byström / A. Deirdre J. Scadden / Michael Jantsch / Valérie de Crécy-Lagard)
- **RNA Editing and RNA Interference**
  (*Brenda Bass* / Robert Reenan / Gordon Carmichael / Mary O'Connell)

NEW! RNA EDITING (GRS)
Editing and Modification of RNA and DNA

Jan 8-9, 2011
Hotel Galvez, Galveston, TX
Chair: Joseph Whipple

The Gordon-Kenan Research Seminar on RNA Editing is a unique forum for graduate students, post-docs, and other scientists with comparable levels of experience and education to present and exchange new data and cutting edge ideas. The focus of this meeting will be on the structure, function and specificity of RNA editing and modification, as well as on the evolution and biological roles of RNA editing and modification systems. An introductory session will feature a discussion of new technologies for the analysis of editing and modification.

- **Speakers:** To be selected from submitted abstracts
- **Discussion Leaders:** To be selected from submitted abstracts
- **Keynote Speakers:** Pat Limbach, "RNA Spell Checking: Approaches for Identifying Editing and Modification Sites"

SALIVARY GLANDS & EXOCRINE BIOLOGY

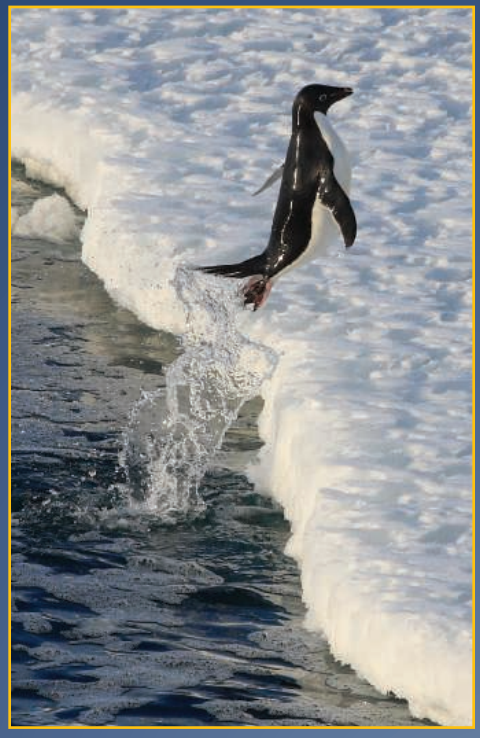
Feb 6-11, 2011
Hotel Galvez, Galveston, TX
Chairs: Matthew P. Hoffman & Masataka Murakami
Vice Chairs: Indu S. Ambudkar & Maria Kukuruzinska

- **Keynote Presentations**
  (*Maria A. Kukuruzinska* / Kenneth M. Yamada / Ray J. MacDonald / Elaine Fuchs)
- **Exocrine Glycobiology**
  (*Sarah M. Knox* / Larry Tabak / Kelly TenHagen / Maria A. Kukuruzinska / J. Michael Pierce)
- **Tumor Biology, Diseases, and Diagnostics**
  (*David T. Wong* / Kirsten H. Limesand / V.P. Eswarakumar / John McDevitt)
- **Signal Transduction and Exocrine Gland Function**
  (*David Yule* / Lily Jan / Jim Putney / Hiroshi Sugiya / Gary Weisman / Akihiko Tanimura)
- **Exocrine Epithelial Biology**
  (*Catherine E. Ovitt* / Sarah M. Knox / Fei Liu / Steven Leach)
- **Systems Biology**
  (*Melinda Larsen* / James Sneyd / Ivan T. Rebustini / Kasia A. Rejniak)
- **Inflammation and Autoimmunity**
  (*Darlene Dartt* / Gabor G. Illei / Seunghee Cha / Hiroshi Ishiguro)
- **Molecular Mechanisms of Exocrine Secretion**
  (*Mary E. Reyland* / Roberto Weigert / Sarah F. Hamm-Alvarez / Debbie J. Andrew / Shmuel Muallem)
- **Progenitor, and iPS Cells**
  (*Indu S. Ambudkar* / Tetsuya Kawakita / Rob P. Coppes / Bruce Baum)

NEW! SIGNAL TRANSDUCTION WITHIN THE NUCLEUS

Feb 27 - Mar 4, 2011
Four Points Sheraton / Holiday Inn Express
Ventura, CA
Chairs: Vytas A. Bankaitis & Ali Shilatifard
Vice Chairs: Mike P. Rout & Pascale Zimmermann

- **Keynote Presentation: The Unfolded Protein Response**
  (*Vytas A. Bankaitis* / Peter Walter)
- **Stress Signaling**
  (*Vytas A. Bankaitis* / Randal Kaufman / Christopher Nicchitta / Jayraj Acharya / Anne Brunet)
- **Nuclear Organization**
  (*Christopher Nicchitta* / Thomas Misteli / Robert Goldman / Sigfried Musser / Katherine Borden)
- **The RNA Polymerase II and Transcription**
  (*Andreas Ladurner* / Andreas Ladurner / Jim Goodrich / Bing Rin)
- **Transcriptional Regulation by RNA Polymerase II and Chromatin**
  (*Ali Shilatifard* / Danny Reinberg)
- **Signaling to the Nucleus**
  (*Jayraj Acharya* / Alan Hinnebusch / Brenda Andrews / Shinya Kuroda)
- **Nuclear Positioning of Chromatin and the Regulation of Gene Expression**
  (*Ramin Shiekhattar* / Susan Gasser / Danish Moazed / Sue Jaspersen)
- **RNA, Chromatin and Nuclear Signaling**
  (*Sue Jaspersen* / Ramin Shiekhattar / Shelley Berger / Jerry Workman)
- **Nuclear Inositide Signaling**
  (*John York* / Susan Wente / Nal Divecha / Lucio Cocco)



An Adélie Penguin leaps from the water onto sea ice near Cape Royds, McMurdo Sound, Antarctica. Photo by Brett Heimlich. Submitted by Patricia Yager, Chair, Polar Marine Science GRC.

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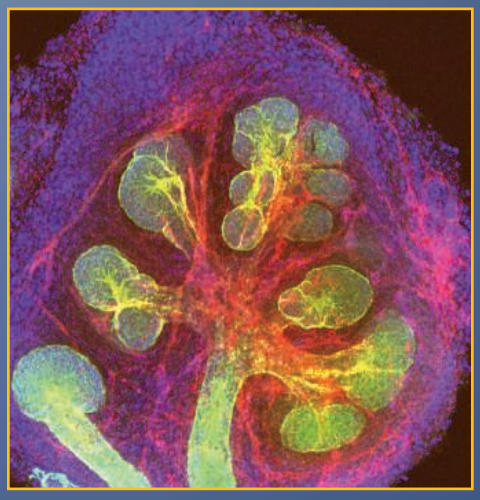


Developing mouse submandibular and sublingual salivary glands undergoing branching morphogenesis. Whole-mount image. The epithelium is stained in green, the blood vessels are red and the nuclei are blue. Submitted by Matthew P. Hoffman, Chair, Salivary Glands & Exocrine Biology GRC.

NEW! STEM CELLS & CANCER

Feb 20-25, 2011
Ventura Beach Marriott, Ventura, CA
Chair: Catriona Jamieson
Vice Chair: Andreas Trumpp

- **Self-Renewal and Cancer**
  (Hans Clevers / Roel Nusse / Tannishtha Reya)
- **Hematopoietic Stem Calls and Cancer**
  (Emmanuelle Passegue / David Traver / Connie Eaves)
- **Reprogramming and Cancer**
  (Robert Wechsler-Reya / Tom Look / Maarten Van Lohuizen)
- **Solid Tissue Stem Cells and Cancer**
  (Jane Visvader / Irv Weissman / Catherine O'Brien)
- **Niche Signaling and Stem Cell Control**
  (Amy Wagers / Toshio Suda)
- **Stem Cell Profiling and (Epi)genomics**
  (Carlo Croce / Leonard Zon)
- **Therapeutics Against Cancer Stem Cells**
  (Dennis Carson / Alan Trounson / Jeremy Rich)

NEW! STOCHASTIC PHYSICS IN BIOLOGY

Jan 23-28, 2011
Four Points Sheraton / Holiday Inn Express
Ventura, CA
Chair: Ken Dill
Vice Chair: Hong Qian

- **Are There Principles of Noise and Networks in Biology?**
  (*Mans Ehrenberg* / Alex van Oudenaarden / Kim Sneppen / Adam Arkin)
- **Bifurcations & Clocks**
  (*Albert Goldbeter* / Steven Altschuler / Rong Li / Wallace Marshall)
- **Foundational Principles of Stochastic Dynamics**
  (*Michael C. Mackey* / Kings Ghosh / Aaron Dinner / Pieter Rein ten Wolde)
- **On Single Molecules & Single Cells**
  (*David Bensimon* / Carlos Bustamante / Alex Mogilner / Sunney Xie)
- **Noise and Control in Gene Expression and Signaling**
  (*Oscar Kuipers* / Hao Ge / Jane Kondev / Tobias Meyer)
- **Synthetic Gene Circuits**
  (*George Oster* / Christopher Voigt / Michael Elowitz / Eugene Shakhnovich)
- **Network Structure and Dynamics**
  (*Eugene Stanley* / Yuhai Tu / Hana El-Samad / Jin Wang)
- **Dynamics in Cell Biology**
  (*Rob Phillips* / Johan Paulsson / Ed Munro / Linda Kenney)
- **Cellular and Network Evolution**
  (Marc Kirschner / Terry Hwa / Philippe Cluzel / Stan Leibler)

NEW! TROPICAL INFECTIOUS DISEASES
From Bench to Field

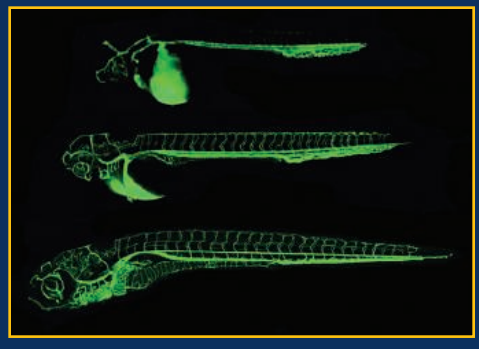
Mar 13-18, 2011
Hotel Galvez, Galveston, TX
Chair: Marcelo Jacobs-Lorena
Vice Chair: David L. Sacks

- **Keynote Presentation: Perspectives on Vaccine Discovery and Development**
  (Adel Mahmoud)
- **Keynote Presentation: Moving House - Invasion and Remodelling of the Host Erythrocyte by *P. falciparum***
  (Alan Cowman)
- **Cholera**
  (*Matthew Waldor* / Matthew Waldor / John Mekalanos / Andrew Camilli / Steve Calderwood / Gary Schoolnik)
- **Ricketsia**
  (*Abdu Azad* / Ulrike Munderloh / Yasuko Rikihisa / Daniel Voth)
- **Leishmania**
  (*David Sacks* / David Sacks / Marlene Boelart / Nicolas Fasel / Lynn Soong / Alain Dessein)
- **African Trypanosomiasis**
  (*Serap Aksoy* / Serap Aksoy / James Bang / Philippe Solano)
- **Arboviruses**
  (*Scott Weaver* / Scott Weaver / Stephen Whitehead / George Dimopoulos / Bill Black / Amy Morrison)
- **Filaria**
  (*Thom Nutman* / Elodie Ghedin / Sara Lustigman / Thom Nutman)
- **Malaria**
  (*Ricardo Gazzinelli* / Brendan Crabb / David Fidock / XZ Su / Ricardo Gazzinelli / Jim Kazura)
- **Keynote Presentation: How to Move from Bench to Field to Utilization: Some Critical Lessons**
  (Robert Ridley)
- **Keynote Presentation: Research with the End in Mind - How the Disease Control Agenda Raises the Challenge for Research**
  (Regina Rabinovich)

VASCULAR CELL BIOLOGY

Feb 20-25, 2011
Four Points Sheraton / Holiday Inn Express
Ventura, CA
Chair: Martin A. Schwartz
Vice Chair: Timothy T. Hla

- **Keynote Presentations: Vascular Development in Zebrafish**
  (*Martin Schwartz* / Didier Stainier / Brant Weinstein)
- **Vascular Development**
  (*Luisa Arispe* / Anne Eichmann / Eckart Iammert / Vicki Bautch)
- **Vascular Patterning**
  (*Mike Simons* / Holger Gerhardt / Shayne Pierce-Cotler)
- **Endothelial Junctions and Permeability**
  (*Elisabetta Dejana* / Dietmar Vestweber / Susan Quaggin / Mark Ginsberg)
- **Intercellular Interactions**
  (*Ken Walsh* / Brant Isakson / Joe McCarty)
- **New Signaling Pathways I**
  (*Tim Hla* / Bill Sessa / Shahin Rafii / Tatiana Byzova)
- **New Signaling Pathways II**
  (*Kathy Griendling* / Michelle Bendeck / Klaus Ley)
- **Mechanotransduction in Vascular Disease**
  (*Anton Horrevoets* / Wayne Orr / Stephanie Lehoux / Robert Poelmann)
- **miRNA and Epigenetic Regulation of Gene Expression**
  (*Gary Owens* / Brian Black / Akiko Hata)



Zebrafish vasculature at several developmental stages. Courtesy of Brant Weinstein (National Institutes of Health), Keynote Speaker, Vascular Cell Biology GRC. Submitted by Martin A. Schwartz, Chair, Vascular Cell Biology GRC.

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Science Careers
From the journal *Science* AAAS

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The Department of Pharmacology seeks highly qualified applicants for two tenure track faculty positions at the Assistant or Associate Professor level. The department has new leadership and is undergoing expansion of its faculty and complete renovation of its research facilities. The department will recruit into any area of its broad research interests including signal transduction, cancer, neuroscience, pain, and cardiovascular disease (**http://www.healthcare.uiowa.edu/pharmacology/**). However, there is a preference for faculty with research interests linking cardiovascular and metabolic diseases. Pharmacology faculty members direct an NIH funded training program for predoctoral students in Pharmacological Sciences and have strong collaborative interactions with colleagues throughout the Carver College of Medicine, Holden Comprehensive Cancer Center and the University. The faculty participate in interdisciplinary training programs including the Cardiovascular Center, as well as the Genetics, Molecular and Cellular Biology, Neuroscience and Medical Scientist Training Programs. Newly remodeled outstanding research space with state of the art shared instrumentation is available. These tenure-track positions include a 12-month salary, benefits and a competitive start-up package. All applicants must have a relevant doctoral degree, with at least 2-3 years of postdoctoral training, a commitment to biomedical education and demonstrate a high level of productivity, strong communication and interpersonal skills. Candidates will be judged on their potential to initiate and maintain a creative, independent research program, their desire to train students and postdoctoral fellows, and to participate in departmental teaching activities.

To apply for this position, visit The University of Iowa website at **http://jobs.uiowa.edu**, requisition **58343**. Applicants should include a CV and a letter of interest that provides a summary of research accomplishments and planned research program. Applicants for the rank of Associate Professor should provide names of three referees. Applicants for the rank of Assistant Professor should ask three referees to directly submit letters on their behalf to Search Committee **#58343** at **pharmacology-search@uiowa.edu**. Review of applicants will begin **October 1, 2010** and will continue until the positions are filled. Anticipated start date is July 1, 2011. Questions may be directed to **Professor Curt D. Sigmund, Head, Department of Pharmacology, phone 319-335-7946**, **pharmacology-search@uiowa.edu**.

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SANFORD HEALTH

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Sanford Children's Health Research Center (SCHRC; Sioux Falls) invites applications from researchers for a full time faculty position at the rank of **Associate Professor** or **Full Professor** within Sanford Research/USD and the Department of Pediatrics of the Sanford School of Medicine at The University of South Dakota. A historic $400 million gift by philanthropist T. Denny Sanford has allowed for expansion of Sanford Research/USD, and development of a two-site program, with locations in Sioux Falls, SD and La Jolla, CA, specifically focused on children's health. The La Jolla site is located within the Sanford-Burnham Institute for Medical Research, allowing for a unique partnership which includes open access to their state of the art core facilities and providing the basis for an integrated, world class, academic pediatric research network.

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Significant institutional support including modern laboratory space and state-of-the-art facilities will be provided in the new Sanford Research Center. In addition, a comprehensive compensation package will be tailored to the individual's qualifications. Candidates should submit a detailed curriculum vitae, description of research experience and future plans, and at least three letters of recommendation. Application materials should be sent to:

David A Pearce Ph.D.
Director, Sanford Children's Health Research Center
Sanford Research/USD
Professor, Department of Pediatrics
Sanford School of Medicine of The University of South Dakota
2301 East 60th Street North
Sioux Falls, SD 57104-0589
Telephone: 605-312-6004 FAX: 605-312-6071
Email:pearced@sanfordhealth.org
http://www.sanfordhealth.org/Research/ResearchCenters/SanfordChildrensHealth/

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BIG THINKING AT SMALL UNIVERSITIES

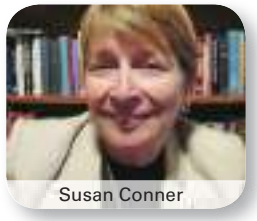
Numerous factors, large and small, come into play when one is deciding where to pursue a research career. Here, faculty members and deans size up their decision to work at a smaller institution and the issues that they face. **By Jacqueline Ruttimann Oberst**

> "At a smaller university, professors tend to go into niches where they're not directly competing with big groups."

Five years ago **Aaron Miller** had a big decision to make. He was flourishing as a staff scientist at the National Institute of Standards and Technology (NIST) in Boulder, Colorado, where he wrote and worked on large research grants. However, with a third kid on the way and aging parents, he felt his hometown calling. Luckily for him one of his old physics professors at Albion College, the small college where he and wife completed their undergraduate studies and near both their families, was retiring and he had the opportunity to apply. He got the job and has never been happier—proof positive that when it comes to research institutions, sometimes smaller is better.

Miller is not alone. Many professors choose to teach and perform research at "small" research universities or colleges—often at huge sacrifices such as longer hours and lower pay. But for them, it's their dream job.

Aaron Miller (left) with student Brian Still



Susan Conner

DEFINING SMALL UNIVERSITIES: BIGGER THAN A BREADBOX?

Ask most people what constitutes a small university or college and you may get as many answers as there are schools. Some choose to define these institutions by their total number of students, others by the number or existence of graduate programs.

Smaller research colleges and universities are informally characterized as those that are not "research 1" universities, nomenclature bestowed by the Carnegie Classifications of Institutions of Higher Learning in 1994 to those institutes who give high priority to research, award 50 or more doctoral degrees each year, and annually received $40 million or more in federal support. This category was renamed in 2000 to "doctoral/research universities-extensive" to "avoid the inference that the categories signify quality differences." The foundation changed the classification again in 2005 and plans another update later on this year, yet despite these series of changes, the defunct term still gets tossed around in academic circles.

Instead of this catch phrase, **Kevin Schug,** an assistant chemistry and biochemistry professor at the University of Texas at Arlington, likens smaller universities and colleges to "an old system in football in which you had 1A teams and several 1AA teams—they're a little step down, but they're not division 2 or 3."

The majority of people, however, would likely agree that a school with an annual research and development budget around or under $50 million is a good cut-off point. This article identified four such universities and colleges: Albion College, The University of Texas at Arlington, Binghamton University, and Harvey Mudd College to explore the differences between small and large universities.

THE FEW, THE PROUD: WHY THEY COME

Why do research professors opt to come to these smaller schools where funding is limited?

"It's often because they had a great experience at small schools in undergraduate school," offers **Susan Conner,** provost of Albion College, a small private college in Michigan solely consisting of 1,700 undergraduate students and an annual research and development (R&D) budget of $630,000. "They had faculty with a huge passion for their research and teaching. They're actually trying to get back to that kind of experience," she adds. "We're not a stepping stone to something else for them."

This certainly was the case for **Roger Albertson,** an assistant biology professor at Albion College. **continued on p. 1380 »**

UPCOMING FEATURES

Focus on Germany—September 24

Diversity 2 (online only)—October 1

Top Employers Survey—October 8

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FACULTY POSITIONS

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Division of Biological Sciences
University of California San Diego
Faculty Recruitment

The Division of Biological Sciences invites applications for 5 new tenure-track or tenured faculty positions with a strong preference for the rank of Assistant Professor. Candidates pursuing innovative research in the described areas are encouraged to apply. The Division of Biological Sciences at UC San Diego (**http://biology.ucsd.edu/index.html**) is committed to academic excellence and diversity within the faculty, staff, and student body.

Systems biology:
The Section of Molecular Biology is seeking applicants in the area of systems and synthetic biology, with a particular focus on interdisciplinary and quantitative approaches to cellular signaling and gene regulation.

Plant systems biology:
The Section of Cell and Developmental Biology invites applications in the field of plant systems biology in areas including, but not limited to, signaling, growth and development, plant-microbe interactions, natural variation, and comparative and quantitative genomics.

Immunology, host-pathogen interactions:
The Section of Molecular Biology invites applicants in the areas of immunology, immunopathology, virology, or host-pathogen interactions.

Cell biology:
The Section of Cell and Developmental Biology wishes to recruit a future colleague who combines the unique strengths of cell biology with cross-disciplinary approaches that might include genomic, proteomic, imaging and system network analysis, to understand how cells function and behave.

Molecular biology, epigenetics:
The Section of Molecular Biology invites applicants with research interests in any area of molecular biology, though preference will be given to those who have a particular focus on epigenetics, epigenomics, and RNA biology.

The successful candidates are expected to have a broad interest in their chosen field, and to complement existing strengths in the Division. All candidates must have earned a Ph.D., M.D., or equivalent degree, and have demonstrated excellence and creativity in research and scholarship. The successful candidate is also expected to participate in the graduate and undergraduate teaching curricula. Preference will be given to candidates with experience in equity and diversity with respect to: teaching, mentoring, research, life experiences, or service towards building an equitable and diverse scholarly environment. The level of appointment will be commensurate with qualifications and experience. Start-up funds will be provided to establish a competitive research program, and salary will be based upon the University of California pay scale.

Complete applications received by **November 1, 2010**, will be assured of consideration. Interested applicants must submit cover letter, curriculum vitae, a statement of research, a statement of teaching, contact information for 3-5 references and a personal summary statement describing their past experience and leadership in equity and diversity and/or their potential to make future contributions in the field. Applications must be submitted through the University of California San Diego's Academic Personnel RECRUIT System at **https://apol-recruit.ucsd.edu/**. Further details about the required application material can be found at: **http://biology.ucsd.edu/jobs/ladder_info.html**.

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with a strong institutional commitment to excellence through diversity.

"For me, it became not do I have what it takes, but what is my true passion and how can I best contribute to this world."
—Roger Albertson

"A community college teacher saw things in me that I didn't see in myself. He helped shape my character," he says. As such Albertson was looking for a way to give back. He sensed, however, that many primary investigators consider it "a step down for people who can't make it in a 'research 1' school." But after much introspection and recognizing his own aptitude for teaching and relating to the students, Albertson concluded that, "for me, it became not do I have what it takes, but what is my true passion and how can I best contribute to this world?"

Another reason, states **Pamela Jansma,** dean of the College of Science at The University of Texas at Arlington, a mid-size university comprising around 30,000 undergraduate and graduate students and an annual R&D budget of $52 million, is that "people choose to come if they felt the environment was less stressful in terms of the pressure to raise external funding and publish."

Schug shares this same sentiment. "When successful in obtaining grants, it's easier to become a bigger fish in a smaller pond," he says. "With success comes respect a little bit earlier, especially in a school our size."

Gerald Sonnenfeld, vice president for research at Binghamton University, another midsized university with around 15,000 graduate and undergraduate students and an annual R&D budget of $44.5 million, offers a quality versus quantity argument. "The quality of what we do here I would put up against any other university," he says. "It's just we don't do it in as many areas as a larger university would do."

Supporting this argument is **Wayne Jones,** an inorganic and materials chemistry professor and department chair at Binghamton University. "Larger universities are more rigid and have lots of infrastructure and lots of redundancy," he says. "This is different at smaller universities where one has to struggle to get the critical mass to do research. However, this shortage provides lots of opportunities to do interdisciplinary research, which, in my opinion, is where the most exciting science can be found."

For others, the choice is one of pride explains **Kerry Karukstis,** former president of the Council on Undergraduate Research and chemistry professor at Harvey Mudd College, a private California college with 750 undergraduates and annual R&D expenses of $2.3 million, "For faculty at undergraduate institutions, the choice is deliberate: For us, there is no greater honor than to have the accolade 'teacher-scholar' associated with our name."

FUNDING: ONE SIZE FITS ALL?

When it comes to research funding, institutional size does not matter, according to Conner. "Everybody's pretty much in the same pot," she says. To increase a university's funding chances from this limited supply, she adds, "You want some faculty who have grant experience because they know how to write grants and can mentor others from their experience. Also, successfully obtaining grants creates a track record, thus enabling researchers to obtain even more grants."

Most faculty members in the sciences receive startup funds ranging from $10,000 to $70,000 to start up their lab. However, once settled, the faculty members must venture forth and accumulate their research nest egg. These foragings typically involve federal institutions such as the U.S. Departments of Energy and Defense, the National Institutes of Health (NIH), and the National Science Foundation (NSF).

Among the highly sought-after grants are the NIH's Academic Research Enhancement Award (AREA) and the NSF's Research Undergraduate Institute (RUI) grant. Both are extremely competitive and selective; only the top 10 to15 percent of applications receives funding. Even more daunting: These grants, while offered solely to undergraduate institutions, do not distinguish smaller universities from larger and more research-experienced institutions.

"We're out there competing with everybody," comments **Robert Drewell,** an associate professor of biology at Harvey Mudd College.

The funding situation forces institutions to be creative and seek other sources of support from foundations like the Howard Hughes Medical Institute (HHMI) or private companies. The American Chemistry Society's Petroleum Research Fund, for example, lends a hand to many faculty researchers at Albion. Similarly, The Welch Foundation provides funding for the chemistry and physics departments at The University of Texas at Arlington. Situated near IBM's hometown, Binghamton's research allowance partially stems from the electronics companies in the area.

MORE FOR LESS: WORKLOAD BALANCE

For most professors teaching is their full-time job—they do research solely on a part-time basis.

Although the teaching load varies from college to college, ranging from one to three classes and/or laboratories per semester, for the most part, undergraduate professors have the summer off from their teaching duties. This is the period during which the bulk of their research gets done.

Some, however, multitask during the semester.

"Since there's not much time to do research during the semester I usually bring it into the teaching labs," says Albertson. It also serves another purpose for him: to identify which undergraduate(s) would like to work in his lab and do research for academic credit.

Choosing an undergraduate student as a research assistant—as well as a research project—can be tricky, notes **Alex Weiss,** professor and associate chair of physics at The University of Texas at Arlington.

"They have a different way of working," Weiss says. "Doctoral students provide a lot of ideas, go to the literature themselves, and contribute to the direction of research—they are not just hands-on. Undergraduates and masters students are mostly doing the research under the director supervision of the professor—the amount of research done this way is limited."

As such, he adds, "at a smaller university, professors tend to go into niches where they're not directly competing with big groups. One can't jump on the bandwagon since **continued on p. 1382 »**

15 NEW FACULTY in 5 NEW AREAS

The Wisconsin Institute for Discovery (WID) announces multiple faculty openings in each of five research theme areas:

TISSUE ENGINEERING SCAFFOLDS will advance the science and engineering of manufacturing scaffolds with the aid of nanotechnology. It will build a library of scaffolding materials and cost-effective, mass-production methods that will work for a wide range of cell types in an array of in-vitro and in-vivo applications.

EPIGENETICS will focus on the molecular, chemical and physical basis underlying epigenetic mechanisms and will serve as the physical and intellectual center on campus that will catalyze interdisciplinary collaborations involving basic and translational research in epigenetics.

LIVING ENVIRONMENTS LABORATORY is an interdisciplinary team that will work together to accelerate the design and deployment of technologies to support health care in the home. Using physical and simulated environments including a virtual reality CAVE™ and a design development lab we hope to inspire and stimulate designers of home health care products, new materials for health, and new devices for personal care.

OPTIMIZATION aims to develop and apply optimization technology to systems-level problems emerging in science and engineering applications in an interdisciplinary, integrative, and collaborative fashion.

SYSTEMS BIOLOGY will advance the frontiers of knowledge by promoting synergistic research, education, and outreach at the interfaces of experimental, computational and evolutionary biology. Areas of special interest include virus-host and microbe-host interactions, innate and adaptive immunity, and ecological and evolutionary dynamics.

The Wisconsin Institute for Discovery will be the home of world-class interdisciplinary biomedical research spanning the fields of bio-, nano- and information technologies, and will occupy a state-of-the-art building opening in December 2010. In addition to WID, this innovative facility will house the privately-funded Morgridge Institute for Research, feature a Town Center with unique opportunities for public science education, and has been designed to prompt interactions among researchers from diverse disciplines. The goals of the institutes are to improve human health and well-being through breakthrough scientific research, and to enhance the University of Wisconsin–Madison's already considerable strengths in interdisciplinary research.

The University of Wisconsin-Madison is a world-class academic institution with an international reputation for basic, applied and cross-disciplinary research. It attracts scholars and students at all levels from around the world. Nationally, UW-Madison ranks fourth among all U.S. universities for research and development expenditures, exceeding $950 million annually. Madison, Wisconsin is surrounded by beautiful lakes and ranks nationally among the most desirable places to live.

WISCONSIN INSTITUTE FOR DISCOVERY

WISCONSIN UNIVERSITY OF WISCONSIN–MADISON

See our website for more details and to apply: www.discovery.wisc.edu/wisconsin/careers

DEPARTMENTS

Including but not limited to: Bacteriology, Biochemistry, Biomedical Engineering, Biomolecular Chemistry, Biostatistics & Medical Informatics, Botany, Chemical & Biological Engineering, Chemistry, Civil & Environmental Engineering, Computer Science, Design Studies, Electrical & Computer Engineering, Genetics, Industrial Engineering, Mathematics, Mechanical Engineering, Medical Genetics, Medical Microbiology, Molecular, Cell, and Developmental Biology (in formation), Nursing, Oncology, Pathobiological Sciences, Physics, Statistics, Zoology.

UW-Madison is an equal opportunity/affirmative action employer. We promote excellence through diversity and encourage all qualified individuals to apply.

"People choose to come if they felt the environment was less stressful in terms of the pressure to raise external funding and publish."
—Pamela Jansma

one doesn't have the resources to beat out the MITs, Caltechs, and Cornells. You have to pick your research topics carefully."

Because teaching is given first priority in smaller research universities, some institutions struggle with encouraging professors to obtain external grants while maintaining their teaching requirements. Most universities reduce the teaching loads for those professors who bring in a significant amount of research funding by either lowering the number of classes they have to teach per semester or allowing the professor to "buy out" of their teaching requirement. In the latter option, teachers use part of their grant money as their teaching salary, thereby allowing the university to use the teaching salary it would normally pay these professors to hire class lecturers.

SAFETY IN NUMBERS: COLLABORATIONS

Balancing research and teaching can be tricky for university professors, regardless of whether they're from big or small universities.

Aaron Miller, an associate professor in the Department of Physics at Albion, succinctly sums up the research/teaching balance conundrum: "How do you stay up in your field when you can only put a quarter of your year into it?" he says. "That's the real challenge."

Typically, Miller says, professors perform side projects that are less relevant to the scientific community and maintain collaborations with larger universities and corporations for more high-profile research. Miller, for instance, does contractual work at larger institutions such as Northwestern University, University of Virginia, and NIST-Boulder (the latter at half the salary he used to get when he worked there full-time).

The tools needed for research can also be lacking in smaller research universities, thus further encouraging collaborations. Albertson conducts a portion of his summer research with his collaborators at the University of California Santa Cruz so that he can use their confocal microscope—an expensive piece of equipment that his school does not have. Similarly, while Schug has mass spectrometry instrumentation in his laboratory, the University currently lacks a core mass spectrometry facility. Core facilities are key infrastructure components, and when they are missing, forward progress in some research areas can be impeded.

"Collaborations are a way for people at smaller places to get around the scale problem," says Weiss.

Despite working fewer hours on their research and with fewer people—typically a handful of undergraduates and graduate students—most of the professors felt that their publication rate would not vary whether they were in a larger versus smaller university.

Some, however, felt that in the publish or perish environment of research, there is safety in numbers.

FEATURED PARTICIPANTS

Albion College
www.albion.edu

American Chemical Society
www.acs.org

Binghamton University
www.binghamton.edu

Council on Undergraduate Research
www.cur.org

Harvey Mudd College
www.hmc.edu

Howard Hughes Medical Institute
www.hhmi.org

National Institutes of Health: Academic Research Enhancement Award Grant
www.grants.nih.gov/grants/funding/area.htm

National Institute of Standards and Technology
www.nist.gov

National Science Foundation
www.nsf.gov

Northwestern University
www.northwestern.edu

The Carnegie Classification of Institutions of Higher Education
classifications.carnegiefoundation.org

The Welch Foundation
www.welch1.org

U.S. Department of Energy and Defense
www.energy.gov

University of Texas at Arlington
www.uta.edu

University of Virginia
www.virginia.edu

"Without continued collaborations, I would not get many publications at all," says Miller.

Still many point out that despite the slower pace and limited supplies and time, the quality of the research is the same regardless of the quantity of papers produced.

Yet, Karukstis points out, "Our work is published in the same peer-reviewed journals."

CONCLUSION: GOOD THINGS COME IN SMALL PACKAGES

"There are pluses and minuses to working in a small institution," says Weiss.

Some, like Jones, feel that it is a call of duty, "Right now the United States struggles getting more students interested in pursuing careers in science," he says. "The key going forward is to find ways to get more students excited and interested in science and engaged in the process of discovery. It will take all types, sizes, and shapes of universities to sustain our technology work force and solve the next generation of problems."

Certain intangibles need also to be considered.

"The quality of life issue was a major decision for us," says Miller. "That's hard to weigh but it's significant. We were looking for a way to get back to a small environment where we can be highly involved in our kids' educations, but can still be involved in doing some world-class research."

For Miller, and many other faculty members, their decision to pursue a career at a smaller research university was an easy one.

Jacqueline Ruttimann Oberst is a freelance writer living in Chevy Chase, Maryland.

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CREDIT: UT ARLINGTON/UNIVERSITY COMMUNICATIONS

EMBL

The European Molecular Biology Laboratory is searching for Group Leaders. EMBL offers a highly collaborative, uniquely international culture. It fosters top quality, interdisciplinary research by promoting a vibrant environment consisting of young, independent researchers with access to outstanding graduate students and postdoctoral fellows. EMBL is an inclusive, equal opportunity employer offering attractive conditions and benefits appropriate to an international research organisation.

Research Group Leader Opportunities
at EMBL Heidelberg, Germany

CELL BIOLOGY & BIOPHYSICS

The Cell Biology and Biophysics Unit takes an interdisciplinary approach to cell biology where biologists work closely together with physicists and chemists. As a result, the highly collaborative mix of groups covers a broad range of technologies, including advanced microscopy, molecular cell biology, biochemistry and genetics to modelling and computer simulations as well as chemical biology. The research focuses on understanding the principles underlying the self-organisation and function of complex and dynamic cellular structures, including the nucleus, cytoskeleton and endomembrane system, in the context of single cells and developing organisms.

GROUP LEADER – CELL BIOLOGY & BIOPHYSICS

We seek innovative candidates working on morphogenetic events in living cells. We will consider outstanding candidates in any area of cell biology. We would like to encourage applicants with a strong background in cell biology, physics or chemistry.

GROUP LEADER – DEVELOPMENT OF ADVANCED LIGHT MICROSCOPY METHODS

We are seeking innovative candidates who will develop novel light microscopy-based imaging methods to address cell biological questions in the cellular or organismal context.

Further information about both positions can be obtained from the Head of Unit Jan Ellenberg (jan.ellenberg@embl.de).

Interviews are planned for 17, 18 and 19 November 2010.

GENOME BIOLOGY

The Genome Biology Unit studies the molecular mechanisms by which genetic information is expressed and regulated to yield complex biological systems, and how genetic variation leads to phenotypic diversity. The Unit addresses questions at different scales, ranging from detailed mechanistic studies (using genetics, biochemistry and cell biology) to genome-wide studies (using functional genomic, proteomic and computational approaches). This powerful combination enables the Unit to dissect and model complex processes going from genotype to phenotype.

GROUP LEADER – GENOME BIOLOGY

This group leader position provides a very competitive package to support an independent research group in an excellent scientific and highly collaborative environment. We particularly encourage candidates with experience in global aspects of epigenetic and chromatin biology, gene expression regulation, stem cell biology or synthetic biology to apply, but welcome candidates with demonstrated excellence in any area of genome biology.

Further information about this position can be obtained from the Heads of Unit Eileen Furlong (eileen.furlong@embl.de) or Lars Steinmetz (lars.steinmetz@embl.de).

Interviews are planned for 22, 23 and 24 November 2010.

APPLICATION INSTRUCTIONS

Please apply online through **www.embl.org/jobs** and include a cover letter, CV and a concise description of research interests & future research plans. Please also arrange for 3 letters of recommendation to be emailed to **references@embl.de**.

Information on Group Leader appointments can be found under **www.embl.org/gl_faq**. Please note that appointments on fixed term contracts can be renewed, depending on circumstances at the time of the review.

www.embl.org

Science Careers online @sciencecareers.org
FACULTY POSITIONS

F A I R F I E L D U N I V E R S I T Y

Assistant Professor of Biology: Animal Physiology

The Department of Biology at Fairfield University invites applications for a tenure-track Assistant Professor position in biology beginning fall 2011. Applicants are expected to have a Ph. D. in the Biological Sciences, a strong commitment to excellence in undergraduate teaching, and potential for developing an active and sustainable research program.

The area of specialty should be Animal/Human Physiology with preference given to candidates with research and teaching interests in physiology at the organismal level. Applicants should be prepared to teach undergraduate courses including participation in the introductory biology series, human anatomy and physiology for biology majors and upper division courses in their area of expertise. Areas of specialization of particular interest to the department include, but are not limited to: Neurophysiology, Reproductive Physiology, Nutritional/Metabolic Physiology, and Kinesiology. The teaching load is three courses each semester. The candidate will join a vibrant and diverse department consisting of thirteen full-time faculty members representing a range of specialties across the biological sciences. The candidate will be expected to engage undergraduates in an active research program related to their field.

Fairfield University is a Jesuit, Catholic institution, consistently ranked as a top comprehensive university in New England and located in the scenic shoreline community of Fairfield, CT, one hour from New York City along Long Island Sound. Our six Colleges and Professional Schools enroll approximately 3,500 undergraduate and 1,200 graduate students, developing intellectual potential in the Jesuit tradition. Review of applications will begin immediately; for full consideration all material must be submitted by Sept 30, 2010. The salary and the benefits for the position are competitive. Applicants should submit curriculum vitae, graduate transcript, statements of both teaching philosophy and research interests, representative reprints of scholarly work, and three letters of reference. These should be sent to: Dr. Brian Walker, Chair, Department of Biology, Fairfield University, Fairfield, CT 06824. The full ad may be viewed at http://www.fairfield.edu/academic/aca_fac_openings.html. No electronic applications will be accepted.

Fairfield University is an Equal Opportunity/Affirmative Action employer, committed to excellence through diversity, and, in this spirit, particularly welcomes applications from women, persons of color, and members of historically underrepresented groups. The University will provide reasonable accommodations to all qualified individuals with a disability. Also, in accordance with the federal Jeanne Clery Disclosure of Campus Security Policy and Campus Crime Statistics Act, the University annually collects and makes publicly available information about campus crimes and other reportable incidents (www.fairfield.edu).

Fairfield UNIVERSITY

Yale

Faculty Position
Department of Cell Biology
Yale University School of Medicine

The Cell Biology Department seeks exceptional candidates at the rank of Assistant and Associate Professor who wish to engage in independent research programs in the field. Successful candidates will have Ph.D., and/or M.D. degrees and a demonstrated record of originality and productivity in research during graduate training and/or post-doctoral research, as well as well-formulated plans for independent research. Although the focus is on tenure-track junior faculty appointments, applicants for senior faculty ranks may also be considered. The Department is undergoing a major expansion under the Chair, Dr. James E. Rothman. Exceptional candidates in all areas of cell biology will be considered.

Please email your CV with a list of publications, a summary of doctoral research [1 page], a summary of postdoctoral research [max. 2 pages], and a research plan [max. 3 pages], along with the names and addresses (including email) of three potential references by **October 25, 2010** to: **cellbio.search@yale.edu**.

Applications from, or nominations of, women and minority scientists are encouraged. Yale is an Affirmative Action/ Equal Opportunity Employer.

OPEN FACULTY POSITIONS INSTITUTE OF MOLECULAR BIOLOGY ACADEMIA SINICA, TAIWAN, ROC

Tenure-track faculty positions are open for highly qualified individuals to establish independent research programs **in the broad area of molecular and cellular biology**. Applicants should hold a Ph.D. degree or its equivalent, and postdoctoral research experience is preferred. Successful candidates will be appointed at the levels of **Assistant, Associate,** or **Full Research Fellows** (equivalent to academic ranks of Assistant, Associate and Full Professors at universities), and receive a generous multi-year start-up package, followed by annual intramural support.

The Institute of Molecular Biology at Academia Sinica **(http://www.imb.sinica.edu.tw/en)** provides an active and stimulating research environment, is well supported by both extramural and long-term intramural funding, and features several core facilities (imaging, microarray & RNAi, electrophysiology, FACS, bioinformatics and mouse facilities) that provide state-of-the-art resources and key technical expertise to the Institute's research community. Recent research works were published in top journals such as Science, Nature, and Cell. Currently three Ph.D. programs, with one recruiting international students, are formally affiliated with the Institute. English is the official language for regular seminars and most of the lectures at the Institute, and proficiency in Chinese language is not a prerequisite for application.

Applicants should send their Curriculum Vitae, a description of past research accomplishments and future research interests, and arrange for three letters of recommendation to be sent directly to:

Dr. Meng-Chao Yao, Director
c/o Ms. Vivi Chiang
Institute of Molecular Biology,
Academia Sinica
Taipei, Taiwan 11529, ROC

The selection process will start on **December 15, 2010** until the positions are filled. Further information can be obtained from Ms. Vivi Chiang at **vivi@imb.sinica.edu.tw**

The Rolanette and Berdon Lawrence Bone Disease Program of Texas

BCM Baylor College of Medicine

The University of Texas MD Anderson Cancer Center Making Cancer History

FACULTY POSITIONS IN THE ROLANETTE AND BERDON LAWRENCE BONE DISEASE PROGRAM OF TEXAS AT THE BAYLOR COLLEGE OF MEDICINE

Two positions are available for tenure-track Assistant Professor as part of the Rolanette and Berdon Lawrence Bone Disease Program of Texas (**http://www.bcm.edu/about/gateways/bonedisease.cfm**). The Program is a collaborative program of the University of Texas MD Anderson Cancer Center and the Baylor College of Medicine with participation from all member institutions of the Texas Medical Center (**http://www.tmc.edu**) in Houston, TX. The Program mission is to provide clinical care for metabolic and oncological bone diseases, and to support clinical, translational, and basic research in skeletal development and disease. One position is available for a MD or MD/PhD-trained physician scientist who is board eligible/certified in adult endocrinology with interest in combining clinical care of adult metabolic bone disease with an independent laboratory research program. Primary appointment will be in the Department of Medicine and the Division of Endocrinology (**http://www.bcm.edu/medicine/**). One position is available for a MD or MD/PhD or PhD-trained basic/translational researcher interested in establishing an independent laboratory program in the area of skeletal development and biology. Primary appointment will be in the Department of Molecular and Human Genetics (**http://www.bcm.edu/genetics/**). The Program provides an extensive infrastructure of core facilities in support of skeletal research. Baylor College of Medicine is listed 13th among all U.S. medical schools for National Institutes of Health funding, and No. 2 in the nation in federal funding for research and development in the biological sciences at universities and colleges by the National Science Foundation. Located in the Texas Medical Center, Baylor College of Medicine has affiliations with eight teaching hospitals, each known for medical excellence. The college has total research support of $302 million, with $241 million from federal sources, and more than 90 research and patient-care centers and units. Currently, BCM trains more than 3,000 medical, graduate, nurse anesthesia, and physician assistant students, as well as residents and postdoctoral fellows.

Please send letter of interest describing clinical/research program and curriculum vitae to **Charlotte Cherry, Administrator, ccherry@bcm.edu or One Baylor Plaza Rm R815 Houston, Tx 77030**.

UNIVERSITY OF MICHIGAN

BIOLOGICAL SCIENCES SCHOLARS PROGRAM

For Junior, Tenure-Track Faculty

The University of Michigan announces recruitment for the Biological Sciences Scholars Program (BSSP) to continue to enhance its investigational strengths in the life sciences research programs.

Now entering its 14th year, this Program has led to the recruitment of outstanding young scientists in the areas of genetics, microbiology, immunology, virology, structural biology, pharmacology, biochemistry, molecular pharmacology, stem cell biology, cancer biology, physiology, cell and developmental biology, and the neurosciences. The Program seeks individuals with PhD, MD, or MD/PhD degrees, at least two years of postdoctoral research experience, and evidence of superlative scientific accomplishment and scholarly promise. Successful candidates will be expected to establish a vigorous, externally-funded research program, and to become leaders in departmental and program activities, including teaching at the medical, graduate, and/or undergraduate levels. Primary college and department affiliation will be determined by the applicant's qualifications and by relevance of the applicant's research program to departmental initiatives and focus. All faculty recruited via the BSSP will be appointed at the Assistant Professor level.

APPLICATION INSTRUCTIONS: Please apply to the Scholars Program through the BSSP website at: (http://www.med.umich.edu/medschool/research/bssp/). A curriculum vitae (including bibliography), a three-page research plan, an NIH biosketch, and three original letters of support should all be submitted through the BSSP website. More information about the Scholars Program, instructions for applicants and those submitting letters of recommendation, and how to contact us is located on the BSSP web site: (http://www.med.umich.edu/medschool/research/bssp/). The deadline for applications is Friday, October 29, 2010.

The University of Michigan is an Affirmative Action/Equal Opportunity Employer.

RUTGERS

Faculty Position in Genetics

The Department of Genetics at Rutgers, The State University of New Jersey seeks an outstanding scientist to fill one of several new faculty positions in genetics. Tenure-track or tenured appointment will be made at the Assistant, Associate, or Full Professor level. We are interested in individuals with research interests that will complement and expand our existing strengths, which include, but are not limited to: human genetics, developmental genetics, cellular genetics, population genetics, microbial genetics, epigenetics, cancer genetics, neuro-genetics, and neuropsychiatric genetics. Appropriate candidates will also be considered for appointment to the Human Genetics Institute of New Jersey. Core resources, startup funds, and laboratory space in the newly constructed Life Sciences Building will be provided.

The Department of Genetics is home to nearly 30 faculty who use a broad range of approaches and experimental systems in numerous well-funded research programs. The department is part of a vibrant and interactive life sciences community that includes over 200 faculty in the Departments of Molecular Biology and Biochemistry, Cell Biology and Neuroscience, and the Robert Wood Johnson Medical School. The New Brunswick/Piscataway campus is located in suburban central New Jersey, close to New York City, Philadelphia, beaches, and countryside. For more information on the Department and Rutgers, see: **http://genetics.rutgers.edu/recruitment**.

Candidates must have a Ph.D. and/or M.D., demonstrated record of significant research, the potential to make substantial contributions as an independent investigator, and have a commitment to teaching undergraduate and graduate students. Applicants should submit a CV, a detailed statement of research interests, a teaching statement, and full contact information for three individuals willing to provide letters of reference. Applications should be submitted electronically at **http://genetics-facsearch.rutgers.edu/apply** and inquiries made to **Ms. Sheri Lumpkin, lumpkin@dls.rutgers.edu**. Review of applications will begin **October 15, 2010** and continue until the position is filled.

Rutgers University is an Equal Opportunity/Affirmative Action Employer committed to diversity. Women, minorities, and members of under-represented groups are encouraged to apply.

RUTGERS

Faculty Position in Computational Genetics

The Department of Genetics in the School of Arts and Sciences at Rutgers, The State University of New Jersey seeks an outstanding scientist to complement the existing faculty in computational genetics, moving our program into exciting new areas and expanding our existing strengths. Tenure-track or tenured appointment will be made at the Assistant, Associate, or Full Professor level. Areas of interest include, but are not limited to, bioinformatics, statistical genetics, theoretical or experimental genomics, population or evolutionary genetics, and analysis of complex genetic diseases. Appropriate candidates will also be considered for appointment to the Human Genetics Institute of New Jersey. Core resources and startup funds will be provided. Research space, including wet lab if needed, will be provided in the newly constructed Life Sciences Building.

The Department of Genetics is home to nearly 30 faculty with diverse interests and numerous well-funded research programs, and is part of a vibrant life sciences and computational community. Our computational group collaborates with academic departments and interdisciplinary institutes in the life and computer sciences, statistics, and medicine. The New Brunswick/Piscataway campus is located in suburban central New Jersey, close to New York City, Philadelphia, beaches, and countryside. For more information on the Department and Rutgers see: **http://genetics.rutgers.edu/recruitment**.

Candidates must have a Ph.D. and/or M.D., demonstrated record of significant research, the potential to make substantial contributions as an independent investigator, and have a commitment to teaching undergraduate and graduate students. Applicants should submit a CV, a detailed statement of research interests, a teaching statement, and full contact information for three individuals willing to provide letters of reference. Applications should be submitted electronically at **http://genetics-facsearch.rutgers.edu/applycompgen** and inquiries made to **Ms. Sheri Lumpkin, lumpkin@dls.rutgers.edu**. Review of applications will begin **October 15, 2010** and continue until the position is filled.

Rutgers University is an Equal Opportunity/Affirmative Action Employer committed to diversity. Women, minorities, and members of underrepresented groups are encouraged to apply.

DREXEL UNIVERSITY COLLEGE OF MEDICINE

DEPARTMENT OF PHARMACOLOGY & PHYSIOLOGY

FACULTY POSITIONS

The Department of Pharmacology and Physiology at Drexel University College of Medicine is seeking applications for full-time, tenure-track faculty to fill positions in the disciplines of Pharmacology and Physiology. This initiative continues our effort to attract outstanding candidates to this Department. We have hired six new faculty within the past year and will continue these efforts to build the Department with an emphasis on strong research-based programs. The Department of Pharmacology and Physiology is in the process of continuing to renovate laboratory and support space to accommodate new and existing faculty as part of the overall initiative to enhance the departmental research, its infrastructure, and educational strengths.

We seek outstanding candidates with a demonstrated commitment and the ability to pursue research in a number of areas in Pharmacology or Physiology. Applicants are expected to demonstrate the capacity to establish or transfer an outstanding and scientifically sound research program that will attract and maintain research funding. Candidates should also be committed to training and education at the graduate and medical school levels. Active participation in the development of a collegial and collaborative research environment is expected. Competitive start-up packages are available.

Applications at the Assistant through the Full Professor level will be considered. The specific research areas for individuals interested in a position are not specified but must complement and/or enhance those within the Department. Areas of focus and faculty interests are available on the Departmental website.

The Department of Pharmacology and Physiology is one of four basic science departments within the College of Medicine. Opportunities for collaborative efforts with these departments as well as with the clinical departments, the School of Biomedical Engineering and College of Engineering are ongoing and strongly encouraged, as are collaborations with other institutions and organizations within the Greater Philadelphia Area.

For more information please consult the following websites for Department of Pharmacology and Physiology (**http://www.drexelmed.edu**) and for graduate biomedical and medical education at Drexel University College of Medicine (**http://webcampus.drexelmed.edu/**). Applicants should submit their curriculum vitae, a statement of their current research and future research directions, relevant teaching experience, and the names of three references to **Carolann.Imbesi@Drexelmed.edu**. Review of applications will begin immediately.

UMASS AMHERST

Assistant Professor

The Department of Biochemistry & Molecular Biology invites applications from Ph.D.-level scientists for a tenure-track position at the level of **ASSISTANT PROFESSOR**. We seek candidates with research programs in topics that complement existing Departmental and campus strengths in cellular biochemistry, including signal transduction, membrane biology, metabolism, gene expression and regulation, and cytoskeletal organization. We are particularly interested in individuals who study plant systems. The successful candidate will be expected to contribute to ongoing interdisciplinary programs focused on renewable energy, cellular engineering, and research at the interface of chemistry and biology. He/she will have access to students from several interdepartmental graduate programs and will be expected to participate in teaching at both undergraduate and graduate levels.

The Five College Consortium, comprised of Smith College, Amherst College, Mount Holyoke College, Hampshire College, and the University of Massachusetts Amherst, provides a rich academic and intellectual environment. The Department is strongly committed to increasing the diversity of the faculty, student body, and curriculum.

Applicants should send curriculum vitae, a description of research interests, and arrange for three letters of recommendation to be sent electronically to: Prof. Jennifer Normanly at bmbsearch@biochem.umass.edu or BMB Search, Biochemistry & Molecular Biology, LGRT 913, 710 N. Pleasant St., University of Massachusetts, Amherst, MA 01003. Review of applications will begin October 15, 2010 and continue until the position is filled.

The University of Massachusetts is an Affirmative Action/ Equal Opportunity Employer. Women and members of minority groups are encouraged to apply.

Burnett School of Biomedical Sciences College of Medicine

Faculty Positions in Four Areas: Cancer, Cardiovascular and Metabolic Diseases, Infectious Diseases and Neurodegenerative Diseases

University of Central Florida is expanding its Biomedical Research and Education Program into a new 198,000sq.ft. Burnett Biomedical Science building in the new medical campus. We seek outstanding scientists working on molecular, cellular, physiological, biochemical, or pharmacological approaches to study important problems with relevance to cancer, cardiovascular and metabolic diseases, infectious diseases and neurodegenerative diseases. Faculty at Assistant, Associate or Full Professor level will be considered. Successful applicants must hold an earned doctorate in a discipline appropriate to the school and will be expected to establish a well funded research program, contribute to teaching, and actively participate in MS and PhD programs.

Competitive salaries, startup funds, new laboratories, transgenic animal facilities and access to the new multimillion dollar shared core instrumentation facilities will be provided. Medical campus is part of multibillion dollar biomedical cluster that includes the Burnett School of Biomedical Sciences, the Medical School, Sanford-Burnham Medical Research Institute, Veterans Administration Hospital and Nemours Children's Hospital. Burnett School researchers will have access to the extensive core facilities in the adjacent Sanford-Burnham Medical Research Institute.

The University of Central Florida is the nation's third largest university and ranks third in innovation and patents. It is located in Orlando, a dynamic and progressive metropolitan region, a major player in high-tech industry, and adjacent to a top ranked Research park and a great place to live and work.

Review of candidates will begin on November 1, 2010. Please apply specifying your area of interest, a curriculum vitae, a two page summary of research plans and contact information for three or more references to **biomed@mail.ucf.edu** .

University of Central Florida

The University of Central Florida is an equal opportunity, equal access, and affirmative action employer. As a member of the Florida State University System, all application materials and selection procedures are available for public review.

STANFORD UNIVERSITY

Department of Biology Faculty Position in Ecology

The Department of Biology at Stanford University seeks applicants for a tenure track Assistant Professorship in Ecology. We seek applicants engaged in answering broad basic questions to advance the field of ecology, with a strong emphasis on the combined application of empirical and theoretical approaches, and with experience and interest in field oriented research. We are interested in applicants studying such questions using plants or microorganisms as study systems, but encourage applications from people working on other systems too. Applicants should write a vision statement that goes beyond a précis of the applicant's prior and current research, to outline one or more major unsolved problems in their field of interest, and how they plan to address them.

In addition to the vision statement described above, applicants are requested to provide a cover letter, a curriculum vitae including publication list, a statement of research accomplishments, a description of teaching experience, and three letters of recommendation. Applicants are expected to develop a vigorous research program and to participate in both undergraduate, graduate, and postdoctoral education and training. For information about the Department consult **http://biology.stanford.edu/**.

Interested candidates should apply online at **AcademicJobsOnline.Org (https://academicjobsonline.org/ajo/jobs/341)**. Applicant materials must be received by **November 15, 2010**. The appointment would begin September 1, 2011.

Stanford University is an Equal Opportunity Employer and is committed to increasing the diversity of its faculty. It welcomes nominations of and applications from women and members of minority groups, as well as others who would bring additional dimensions to the university's research, teaching, and clinical mission.

UT SOUTHWESTERN MEDICAL CENTER

CHAIR, DEPARTMENT OF PATHOLOGY
UNIVERSITY OF TEXAS SOUTHWESTERN MEDICAL CENTER DALLAS, TEXAS

The University of Texas Southwestern Medical Center invites applications and nominations for the position of the Chair of the Department of Pathology.

UT Southwestern is at the forefront of many scientific fields, including cancer, genetics, metabolism, heart disease and neuroscience and counts four Nobel laureates, 18 members of the National Academy of Sciences, and 18 members of the Institute of Medicine of the National Academy of Sciences among its faculty.

This is an exciting time for the UT Southwestern Medical Center. A new University Hospital is in the planning stage with expected occupancy in 2015; a new Parkland Hospital will be constructed at the same time. The chair of Pathology and the department of Pathology faculty will play an important role in realizing the opportunities that these new facilities will provide.

We seek a recognized leader with an outstanding academic background, including strong clinical and research credentials, demonstrated commitment to education, experience in mentoring junior faculty, and proven leadership and management skills. Candidates must have an MD or PhD degree, or equivalent, and must have academic credentials for a tenured faculty appointment at the University of Texas Southwestern Medical School. Board Certification in Anatomic and/or Clinical Pathology is preferred.

Interested individuals should send a curriculum vitae and cover letter to the **Chair of the Search Committee, James K.V. Willson, MD, Pathology Chair Search Committee, c/o Marci Martinez, 5323 Harry Hines Blvd. Dallas, TX 75390-8590, Marci.martinez@utsouthwestern.edu**.

University of Texas Southwestern Medical Center of Dallas is an Equal Opportunity Employer.

UNIVERSITY OF MICHIGAN

Presidential Interdisciplinary Junior Faculty Initiative: Genes, Environment, and Behavior (GEB)

The University of Michigan intends to recruit a cluster of five new faculty members at the rank of assistant professor (tenure-track) whose research programs explore the links between genes, environment, and behavior. Each new hire will have a faculty appointment in one of the following academic departments: Psychology or Molecular, Cellular, and Developmental Biology (in the College of Literature, Science, and the Arts); or Neurology, Human Genetics, or the Molecular and Behavioral Neuroscience Institute (in the Medical School). These faculty, who are expected to interact through this program, will also be integrated into the University's vigorous academic community of behavioral and molecular neuroscientists, developmental and cognitive psychologists, geneticists, and biologists.

To ensure full consideration, all applications should be received by **October 15, 2010** and must be submitted online at **http://www.mcdb.lsa.umich.edu/geb**, where additional information about this program and about the University of Michigan can be found.

Women and underrepresented minorities are encouraged to apply. The University of Michigan is supportive of the needs of dual career couples and is an Equal Opportunity/Affirmative Action Employer.

UNIVERSITY OF CALIFORNIA RIVERSIDE

The University of California, Riverside School of Medicine

seeks to recruit **three** faculty members at the **tenured Associate to Full Professor** level. Successful applicants will be appointed in the Division of Biomedical Sciences, joining a small group of exceptional faculty members who have directed a successful M.D. program in collaboration with UCLA for the past 33 years. The newly-approved School of Medicine will evolve from the current Division and is slated to open in August of 2012. Successful candidates will be expected to bring and maintain a vigorous, well-funded research program and provide research leadership through group development and collaboration with existing faculty, both within and outside of the Medical School. Areas of research within the Division include integrative immunology (vaccine development, neuro-immune, endocrine-immune, host-pathogen interactions), glial-neuronal interactions, cancer biology, cardiovascular disease, and diseases of ion transport. Particular strengths on the campus include genetics, epigenetics, genomics/bioinformatics, microRNAs, vector biology, bioengineering and nanotechnology, and synthetic and analytical chemistry. UCR has several vivaria, including a new one ready for occupancy, and excellent core facilities in genomics, microscopy, and stem cell biology, the latter supporting an emerging focus on campus. Substantial initial complement and research space in a brand new medical research building with a BSL-3 facility is available. The Division of Biomedical Sciences sponsors an innovative Ph.D. program that integrates the core medical curriculum with biomedical graduate training and research. Successful candidates would be expected to teach in the medical curriculum and actively participate in the Biomedical Sciences Ph.D. program.

Position 1: Role of inflammation in the onset or progression of disease, including its role in cancer, metabolic syndrome, and cardiovascular disease, as well as autoimmune and infectious diseases.
Position 2: Molecular mechanisms of CNS neurological disease, including genetic and environmental, causes, and immune- or glial-neuronal interactions in neurodevelopment and neurodegeneration.

For both of these positions, the ideal candidate would utilize one or more mammalian disease models that contribute to investigation of molecular and cellular mechanisms.

Position 3: Population-based health outcomes/effectiveness research, including population-based assessment of health and wellness, assessment of health interventions and health disparity, and access research. We are particularly interested in those individuals experienced in comparable effectiveness research who could analyze site and type of practice variability in the inland Southern California area. Approaches to quantify behaviors, services and tools that could lead to superior patient outcomes and lowered cost of care are also desirable.

All applicants must hold a Ph.D., M.D., or equivalent degree and qualify for appointment at the tenured Associate Professor level. For all three positions, research programs that are particularly applicable to the mission of the medical school are highly encouraged:- *to improve the health of the people of California and, especially, to serve Inland Southern California by training a diverse workforce of physicians and by developing innovative research and health care delivery programs that will improve the health of the medically underserved in the region and become models to be emulated throughout the state and nation.* Applications will be reviewed beginning **October 1, 2010** and the position will remain open until filled. Applicants should send a curriculum vitae, a statement of research accomplishments and goals, and the names of three individuals who will be asked to provide letters of reference once a short list is developed to **Faculty Search Committee Chair (state position 1, 2 or 3), Division of Biomedical Sciences, University of California, Riverside, CA 92521**.

UC Riverside is an Equal Opportunity/Affirmative Action Employer.

UNIVERSITY OF SOUTH CAROLINA
SCHOOL OF MEDICINE

FACULTY POSITION
Pharmacology, Physiology, and Neuroscience

The Department of Pharmacology, Physiology and Neuroscience at the University of South Carolina School of Medicine invites applications for a faculty position at the **ASSISTANT PROFESSOR** level. New faculty members will join a collegial and collaborative department at a university in the midst of an ambitious program to achieve national prominence in research and education. Candidates with research interests that complement the departmental research programs that focus on studying the molecular or cellular mechanisms underlying physiological processes, complex behaviors, or drug action are desirable. Successful candidates will also be expected to participate in medical and graduate teaching. Applicants must have a doctoral degree and postdoctoral experience. Preference will be given to individuals with experience in medical education, funding success and potential, and research interests that enhance departmental programs targeting neurological, neuropsychiatric, cardiovascular, or endocrine disorders. Substantial start-up funds and modern facilities will be provided. The initial appointment is viewed as a non-tenure-track position, with transition into a tenure-track following establishment of a funded, independent research program and demonstration of teaching competency. Exceptional applicants will be considered for immediate appointment on the tenure-track.

Qualified applicants may apply by submitting a single electronic file (PDF or Word) that includes a cover letter summarizing qualifications, curriculum vitae and publication list, a statement of research plans and professional goals, and contact information for four references. The file should be attached to an e-mail message sent to: **Dr. Marlene Wilson** at **e-mail: ppn.search@uscmed.sc.edu** with "PPN Faculty Search" as the subject before December 15, 2010. For more information about the department including our research programs please visit **website: http://ppn.med.sc.edu/.** *The University of South Carolina is an Affirmative Action/Equal Opportunity Employer.*

ASSISTANT PROFESSOR

The Department of Biochemistry at the University of Wisconsin-Madison (**website: http://www.biochem.wisc.edu**) invites applications for a position in biochemistry at the Assistant Professor level. The Department is interested in candidates working at the cutting edge in all areas of biochemistry (e.g., chemical, structural, cellular, developmental and physiological). The University and Department provide an excellent environment for the development of an outstanding research program. The successful candidate will be expected to develop a vigorous, extramurally funded, independent research program, and to participate in the undergraduate and graduate teaching programs of the Department. Applications sent as a single PDF file should include curriculum vitae, list of publications, and a brief summary of accomplishments and directions of future research. Materials should be sent to **e-mail: facultysearch@biochem.wisc.edu.** Three letters of reference should be forwarded by references to the same address with applicant's name in the header. Applications should be completed by October 15, 2010.

ASSISTANT PROFESSORSHIP
in Chemistry
Harvard University

Candidates are invited to apply for tenure-track Assistant Professorships in all fields of chemistry. Candidates should arrange to have three letters of recommendation sent independently and provide curriculum vitae, statement of teaching philosophy, list of publications, and outline of their future research plans. All applications and supporting materials must be submitted via the **website: http://www.chem.harvard.edu.** The deadline for receipt of applications and supporting materials is October 15, 2010.

Harvard University is an Affirmative Action/Equal Opportunity Employer. Applications from and nominations of women and minority candidates are strongly encouraged.

University of Connecticut

ECOTOXICOLOGIST
WILDLIFE or FISHERIES

Department of Natural Resources and the Environment and Center for Environmental Sciences and Engineering seek applicants for a nine-month, tenure-track **ASSISTANT** or **ASSOCIATE PROFESSOR** position, to begin 23 August 2011. We seek a collaborative and multidisciplinary candidate, whose research and teaching focus on field and laboratory measurement of ecotoxicological data as it relates to wildlife or fisheries. Teaching duties include undergraduate and graduate courses in areas of expertise. Doctoral degree required at the time of appointment; postdoctoral experience preferred. Screening will begin 8 October 2010 and continue until the position is filled. More information is available at **website: http://ecotoxicology.uconn.edu.**

Applicants should visit Husky Hire at **website: http://www.jobs.uconn.edu** to upload an application letter, curriculum vitae, statements describing teaching philosophy and research interests, and the names and contact information of three individuals who have been asked to submit letters of reference. Letters of recommendation should be electronically sent directly to the co-chairs of the Ecotoxicology Search Committee (**Drs. John Volin** and **Michael Willig**) via **e-mail: environment@uconn.edu.**

University of Connecticut is an Equal Employment Opportunity/Affirmative Action Employer.

ECOLOGIST

The Department of Biology at the College of William and Mary seeks applications for a tenure-track position at the **ASSISTANT PROFESSOR** level in Ecology with significant contribution to the college's Environmental Science and Policy program (ENSP). The position is open to applicants conducting research in any field or scale of ecology that adds to existing biological and environmental strengths at William and Mary. Preference will be given to individuals working on terrestrial systems. The ideal candidate will have the ability to integrate knowledge across diverse disciplines and levels of biological organization, and possess excellent communication skills that will inspire a bright and highly motivated student body ranging from introductory to graduate students. The successful candidate is expected to establish and maintain an externally funded research program involving both undergraduate and Master's degree students. Teaching expectations are one course per semester and will include an annual upper-division ecology course with a field laboratory component suitable to count towards the ENSP program, an introductory ENSP course on a rotational basis (probably once every three years), and ecology and quantitative courses of interest that would meet the needs of the biology department. Postdoctoral research experience is required, and previous experience teaching undergraduate courses will be viewed favorably. Review begins November 1, 2010 and will continue until an appointment is made. Submit online a letter of application, curriculum vitae, statements of research plans and teaching philosophy, and a list of courses taken/taught relevant to the position as a single PDF document to **http://jobs.wm.edu.** Also arrange for three letters of reference to be sent directly to: **Ecology Search Committee, Department of Biology, The College of William and Mary, P.O. Box 8795, Williamsburg, VA 23187-8795.** Information on the undergraduate and Master's degree programs in the biology department and this position may be obtained at **website: http://www.wm.edu/biology.** Information about the environmental science and policy program can be accessed at **website: http://www.wm.edu/environment.** *The College is an Equal Employment Opportunity/Affirmative Action Employer.*

SYSTEMS NEUROSCIENCE
at Cornell University

The Department of Neurobiology and Behavior (NBB) invites applications for a tenure-track position as **ASSISTANT PROFESSOR** of Neurobiology. Applicants must have a Ph.D. and investigate the neuronal basis of behavior. While the research area is broadly defined, topics of special interest include, but are not limited to, the neuronal basis of decision-making; reward, learning, and memory; and sensorimotor integration. We seek an individual using genetic, optical, computational, and/or physiological tools. She/he will be expected to establish a vigorous, externally funded, internationally recognized research program and to participate and excel in NBB's undergraduate and graduate teaching programs. The successful candidate will join a growing neuroscience and life sciences community on Cornell's main campus in Ithaca, New York. The community includes several new academic units (e.g., Institute of Cell and Molecular Biology, Department of Biomedical Engineering, Department of Biological Statistics and Computational Biology); programs (e.g., Center for Vertebrate Genomics, Center for Comparative and Population Genomics); and core facilities (e.g., Biophysical Imaging, DNA Sequencing and Genotyping, Animal Transgenics); visit **website: http://www.lifesciences.cornell.edu.** For information about the Ithaca area, visit **website: http://www.visitithaca.com/.**

To apply: Send, via electronic mail to **e-mail: tmn3@cornell.edu,** a single PDF of the following materials: Curriculum vitae, statement of research plans, statement of teaching interests, and up to three publications. Please have three letters of reference sent to the same e-mail address. Questions about the search can be directed to: **Professor Joseph Fetcho, Chair, Search Committee, NBB, Seeley G. Mudd Hall, Cornell University, Ithaca, New York 14853–2702. Telephone: 607–254–4340.** Review of applicants begins November 1, 2010.

Cornell is an Equal Opportunity, Affirmative Action Employer. Women and minority candidates are strongly encouraged to apply.

ASSISTANT PROFESSOR or
ASSOCIATE PROFESSOR
University Of Minnesota
The Institute for Translational Neuroscience

The Institute for Translational Neuroscience at the University of Minnesota is seeking to hire one tenure-track faculty member at the Assistant or Associate Professor level to enhance research strengths in neurodegenerative diseases and cognitive aging. This position will be based within the N. Bud Grossman Center for Memory Research and Care, directed by **Dr. Karen Hsiao Ashe,** M.D., Ph.D.

Neuroscientists and physicians with Ph.D. and/or M.D. degrees are eligible to apply. Primary criteria for appointment are superlative scientific accomplishment and the promise of future research impact. Successful candidates must demonstrate the capability to establish a vigorous, externally funded research program, a commitment to medical, graduate or undergraduate education, and leadership through vision and collaborative program development. Of particular interest are candidates with expertise in neuroimaging biomarkers of the earliest stages of Alzheimer's disease in humans or animal models. New faculty will receive substantial recurring salary support, an excellent start-up package, and laboratory space in a newly built, integrated translational research complex that includes state-of-the-art MRI, PET, and microPET facilities.

Applications should be submitted electronically through our Online Application System at **website: http://employment.umn.edu/applicants/Central?quickFind=89475.**

The University of Minnesota shall provide equal access to and opportunity in its programs, facilities, and employment without regard to race, color, creed, religion, national origin, gender, age, marital status, disability, public assistance status, veteran status, sexual orientation, gender identity, or gender expression.

SANFORD HEALTH

ASSISTANT SCIENTIST POSITIONS SANFORD CHILDREN'S HEALTH RESEARCH CENTER

Sanford Children's Health Research Center (SCHRC; Sioux Falls) invites applications from researchers for full time faculty positions at the rank of Assistant Professor within Sanford Research/USD and the Department of Pediatrics of the Sanford School of Medicine at The University of South Dakota. A historic $400 million gift by philanthropist T. Denny Sanford has allowed for expansion of Sanford Research/USD and dynamic development of programs specifically focused on children's health. Sanford Children's Health Research Center (SCHRC) is a two-site campus, with locations in Sioux Falls, SD and La Jolla, CA. The La Jolla site is located within the Sanford-Burnham Institute for Medical Research, allowing for a unique partnership which includes open access to their state of the art core facilities and providing the basis for an integrated, world class, academic pediatric research network.

We seek outstanding scientists with research programs that contribute to molecular understanding and treatment of childhood diseases and developmental disorders. Areas of interest include, but are not limited to: genetics, cell biology, cancer biology, and developmental neuroscience/biology. To augment existing strengths, scientists using various model systems in the study of pediatric disease/developmental disorders or those focused on the study of rare pediatric diseases are encouraged to apply. Successful candidates will have PhD, DVM, MD or MD/PhD degrees and join the energetic and collegial research community at Sanford Research/USD. Candidates will be expected to develop an independent and vigorous extramural research program, complement the interdisciplinary and collaborative nature of the growing SCHRC and promote translational research. The researchers will hold both Sanford Research/USD and Sanford School of Medicine faculty appointments.

Significant institutional support including modern laboratory space and state-of-the-art facilities will be provided in the new Sanford Research Center. In addition, a comprehensive compensation package will be tailored to the individual's qualifications.

Candidates should submit a detailed curriculum vitae, description of research experience and future plans, and at least three letters of recommendation. Application materials should be sent to:

David A Pearce Ph.D.
Director, Sanford Children's Health Research Center
Sanford Research/USD
Professor, Department of Pediatrics
Sanford School of Medicine of
The University of South Dakota
2301 East 60th Street North
Sioux Falls, SD 57104-0589
Telephone: 605-312-6004
FAX: 605-312-6071
Email:pearced@sanfordhealth.org
http://www.sanfordhealth.org/Research/ResearchCenters/SanfordChildrensHealth/

Sanford Health is an Equal Opportunity/ Affirmative Action Employer.

Faculty Positions, Vollum Institute
Oregon Health & Science University, Portland OR

The Vollum Institute (**www.ohsu.edu/vollum**) announces junior faculty positions for outstanding scientists. We are particularly interested in individuals with a research focus in *cell biology, biophysics and molecular structure, molecular and cellular neuroscience, molecular genetics, developmental neurobiology or neuronal cell signaling.* Vollum appointments are full-time research positions with minimal teaching requirements. Ample opportunities are available for collaboration with research units at OHSU (**www.ohsu.edu**) as well as clinical units within the School of Medicine.

We offer attractive start-up packages and the opportunity to work in an outstanding scientific environment. Applicants should have a strong record of research and an interest in training graduate students. OHSU is an equal opportunity/affirmative action employer committed to maintaining diversity in its faculty. Candidates with a Ph.D. and/or M.D. and at least several years of postdoctoral experience should apply by sending an electronic copy of their curriculum vitae, a description of research plans and goals, and three reference letters by **November 1, 2010** to:

Gary L. Westbrook, M.D.
Senior Scientist and Co-Director
Vollum Institute Search
Vollum Institute, L474
Oregon Health & Science University
3181 SW Sam Jackson Park Road
Portland, OR 97239-3098

volljob@ohsu.edu

OREGON HEALTH & SCIENCE UNIVERSITY

UNIVERSITY OF MARYLAND

TWO FACULTY POSITIONS IN ENERGY RESEARCH

The A. James Clark School of Engineering at the University of Maryland is seeking applicants for the **University of Maryland Energy Research Center (UMERC), www.energy.umd.edu**. UMERC is a strategic university initiative that brings together faculty across the campus to advance the frontiers of energy science and technology in the Nation's capitol. It includes and collaborates with the DOE Energy Frontier Research Center "Nanostructures for Electrical Energy Storage", the Center for Environmental Energy Engineering, the Center for Multiscale Plasma Dynamics, the Institute for Systems Research, the Center for Integrative Environmental Research, and the Joint Global Change Research Institute. The Clark School seeks both a senior and junior faculty member:

Full/Associate Professor: This is a senior faculty position with eligibility for the *Herbert Rabin Endowed Chair*. The candidate should have national prominence for their contributions to energy research and have demonstrated success with large multi-disciplinary proposals. If interested, the candidate would also be considered for the position of *Deputy Director of UMERC*. The Deputy Director would work with the Director of UMERC to coordinate energy research across campus and lead large multi-disciplinary opportunities. Possible research areas include but are not limited to: photocatalysis, photovoltaics, catalysis (biofuel and fossil); energy efficiency, harvesting, and storage; energy systems and smart grid technology; and the intersection between energy technology and policy. However, this position is open to the best candidate regardless of specific research focus.

Assistant Professor: This is a tenure-track faculty position within the college. The candidate should have a record of contribution in the energy field commensurate with a junior faculty position. While the area of energy research is open, preference would be given to expertise in electrochemical energy conversion and storage, including research in electrochemical systems, computational materials, materials properties/processing, and electrocatalysis. A 'cluster hire' with the senior faculty position would also be considered.

Appointments for each position will be made in an Academic Department within the College of Engineering that is most commensurate with the interests and expertise of the candidates. Joint appointments will also be considered.

For best consideration, applications should be received by November 12, 2010. Please submit letter of interest, full resume including a list of publications, a statement of research and teaching interests, and the names of at least four references, preferably in PDF by electronic mail to: **Annette Mateus, Coordinator, University of Maryland, UMERC, Rm. 3234, Jeong H. Kim Engineering Building, College Park, Maryland 20742; 301-405-4799 (phone), 301-314-8514 (fax); email: amateus@umd.edu.**

The University of Maryland is an Equal Opportunity, Affirmative Action Employer with a strong commitment to the principle of diversity. Women and minorities are encouraged to apply.

POSITIONS OPEN

Yale

YALE UNIVERSITY
Systems Biology Institute

Yale University, to further the development of its West Campus research enterprise, is seeking **FACULTY** at both **JUNIOR** and **SENIOR** ranks for a new multidisciplinary Systems Biology Institute. Faculty associated with this Institute will have primary appointments in the life science and physical science departments of the Faculty of Arts and Sciences, School of Engineering and Applied Sciences and School of Medicine. Candidates must have a Ph.D. in a relevant discipline and a record of research that demonstrates originality in addressing significant questions in the study of regulatory biology. Relevant research areas include, but are not limited to, functional and comparative genomics, function and evolution of gene regulatory networks, regulation of signal transduction, cell type identity, and the behavior of complex physiological systems. To apply, please submit to **e-mail: kelly.locke@yale.edu** in one PDF file with the subject heading "Systems Biology Search" the following materials: a statement of research interests, complete curriculum vitae, and up to five reprints of published work. Please arrange for three letters of recommendation addressed to: **The Systems Biology Search Committee, c/o Michael Donoghue, Vice President for West Campus Planning and Program Development, 1 Hillhouse Avenue, New Haven, CT 06520.** The review of applications will begin on October 18th, 2010. *Yale University is an Affirmative Action/Equal Opportunity Employer. Yale values diversity among its faculty, students, and staff and strongly encourages applications from women and underrepresented minorities.*

FACULTY POSITION
in CELL and MOLECULAR PHYSIOLOGY

The Department of Cell and Molecular Physiology at Loyola University Chicago, Stritch School of Medicine (see **website: http://www.stritch.luc.edu/depts/physio/index2.cfm**) seeks applicants for a faculty position at the **ASSOCIATE** or **FULL PROFESSOR** level. Applicants with a Ph.D., M.D., or equivalent are expected to maintain a strong and interactive research program. Applicants should have a strong record of research productivity and current extramural support. Applicants whose research complement and extend existing research strengths in cellular and molecular aspects of cell signaling mechanisms in the cardiovascular and aging fields are especially encouraged to apply. Send letter, curriculum vitae including research plans and names of three references to: **Ruben Mestril, Ph.D., Faculty Search Committee Chair, Department of Cell and Molecular Physiology, Loyola University Chicago, 2160 South First Avenue, Building 102, Room 4644, Maywood, IL 60153. E-mail: physiorecruit@lumc.edu.**

Loyola is an Equal Opportunity/Affirming Action Employer.

DUKE UNIVERSITY. The Department of Chemistry invites applications and nominations for a tenure-track position at the **ASSISTANT PROFESSOR** level to begin September 2011. In combination with a commitment to teaching, candidates should have research interests in chemical biology/synthesis; we are particularly interested in candidates who would interface with ongoing university initiatives in systems biology or molecular imaging. Applications received by November 1 will be guaranteed consideration, although extraordinary applicants will be considered after this date. To guarantee consideration, all applicants should provide curriculum vitae, list of publications and description of research interests in PDF format to **e-mail: positions@chem.duke.edu.** Applicants should also arrange to have three letters of recommendation submitted on their behalf electronically to **e-mail: positions@chem.duke.edu.** *Duke University prohibits discrimination and harassment, and provides Equal Employment Opportunity without regard to race, color, religion, national origin, disability, veteran status, sexual orientation, gender identity, sex, or age. Duke is committed to recruiting, hiring, and promoting qualified minorities, women, individuals with disabilities, and veterans.*

POSITIONS OPEN

PRINCETON UNIVERSITY

ASSISTANT PROFESSORSHIP
Ecology, Evolution and/or Behavior

Princeton University's Department of Ecology and Evolutionary Biology plans to hire a tenure-track Assistant Professor. We have broad interests in ecology, evolution, behavior, functional biology, conservation biology, biogeochemistry, and disease dynamics. We seek applicants who pursue research that aims for significant conceptual and/or empirical integration across traditional disciplinary boundaries and who have a strong commitment to teaching. Applicants should write a vision statement, no longer than two pages, that outlines one or more major unsolved problems in their field and how they plan to address them. The vision statement should go beyond a précis of the applicant's prior and current research. Applications, including the vision statement, curriculum vitae, three reprints, and contact information for three references should be submitted online via **website: http://jobs.princeton.edu,** Req **#1000647**. Any questions about the position should be addressed to **Dr. Bryan Grenfell,** the chair of the search committee. Screening of applications will begin 15 October 2010, and will continue until the position is filled.

Princeton University is an Equal Opportunity Employer and complies with applicable Equal Employment Opportunity and Affirmative Action regulations.

VERTEBRATE ECOLOGIST. The Wabash College Biology Department invites applications for a Byron K. Trippet **ASSISTANT PROFESSORSHIP** in **ECOLOGY**. Tenure-track position to start July 1, 2011. Ph.D. and a commitment to excellence in teaching required; teaching experience desirable. Primary expertise should be in ecology, with the ability to teach a course in comparative vertebrate anatomy. Active engagement of undergraduates in an ongoing research program is expected.

In a two-year cycle, responsibilities include teaching lab and field courses in general ecology, comparative vertebrate anatomy, and a course in the applicant's special area of expertise. Also, candidates will be expected to participate in team-taught general biology courses and make periodic contributions to all-college courses. The typical classroom teaching load (including labs) is 12 contact hours per semester.

The Biology Department, with six full-time faculty positions, encompasses molecular biology, organismal biology, and population biology. The department is well-equipped for teaching and research, including ownership of a pond property and the Allee Woods Nature Preserve, a 180-acre forest that is one of Indiana's highest quality natural areas. The Byron K. Trippet Assistant Professorship provides a summer stipend and research support during the first two years. In addition, significant departmental start-up funds are provided along with dedicated resources for research, teaching, and travel support. In addition to local and regional field-sites, in recent years the department has supported field-work for course-related immersion study and research in areas such as Belize, Ecuador, and Peru.

Send a letter of application, curriculum vitae, brief statements of teaching philosophy and research interests, undergraduate and graduate transcripts, and three letters of recommendation by October 22 to: **Dr. Eric J. Wetzel, Chair, Biology Department, Wabash College, P.O. Box 352, Crawfordsville, IN 47933.** Questions may be directed to **e-mail: wetzele@wabash.edu.** Information about the College and Department is available at **website: http://www.wabash.edu.** *Wabash College, a liberal arts college committed to the undergraduate education of men, encourages applications from women and minorities. Equal Opportunity Employer.*

POSITIONS OPEN

UT SOUTHWESTERN MEDICAL CENTER

TENURE-TRACK POSITIONS
The University of Texas
Southwestern Medical Center

ASSISTANT PROFESSORS. The Department of Physiology invites outstanding scientists with Ph.D., M.D., or equivalent degrees to apply for tenure-track Assistant Professor positions. Candidates who use innovative optical, mechanical, electrical, molecular, biological, or computational methods with important applications to physiological systems, ranging from individual genes and proteins to cells and organs are encouraged to apply. However, the scientific excellence of the candidates is more important than the specific area of research.

These positions are part of the continuing growth of the Department at one of the country's leading academic medical centers and will be supported by significant laboratory space on our new campus, competitive salaries, and exceptional start-up packages. The University of Texas Southwestern Medical Center is the scientific home to four Nobel Prize laureates, 18 members of the National Academy of Sciences, and 18 members of the Institute of Medicine. UT Southwestern conducts more than 3,500 research projects annually totaling more than $400 million.

Applicants should submit curriculum vitae, a brief statement of research plans, and arrange to have three letters of reference sent to: **James Stull, Ph.D., c/o Ronald Doris, Department of Physiology, The University of Texas Southwestern Medical Center, 5323 Harry Hines Boulevard, Dallas, TX 75390-9040.** *UT Southwestern strongly encourages applications from women, minorities, and people with physical challenges. An Equal Opportunity Employer.*

ASSISTANT PROFESSOR
Neurophysiology

The Department of Biology and the Neuroscience Program at Amherst College invite applications for a tenure-track position at the Assistant Professor level in cellular neurophysiology, to begin July, 2011. The research program of the successful candidate will be one that can involve undergraduate biology and neuroscience majors. Teaching duties include a laboratory course in neurophysiology, other courses related to the candidate's area, for example a course in general or comparative physiology, and participation in team-taught introductory courses. A completed Ph.D. is required and postdoctoral experience is expected.

Candidates should submit electronically to **website: https://jobs.amherst.edu/view/opportunity/id/249** curriculum vitae and statements of research and teaching interests. Three letters of recommendation addressed to the Neurobiology Search Committee should be submitted to **Tracie Rubeck,** Academic Department Coordinator; **e-mail: trubeck@amherst.edu.** Review of applications will begin October 15, 2010, and continue until the position has been filled. Amherst is a private undergraduate liberal arts college for men and women, with 1,700 students and a teaching faculty of 200. Located in the Connecticut River Valley of western Massachusetts, Amherst participates with Hampshire, Mount Holyoke, and Smith Colleges and the University of Massachusetts in the Five College Consortium. *Amherst College is an Equal Opportunity Employer and encourages women, persons of color, and persons with disabilities to apply. The College is committed to enriching the diversity of its faculty, administration, and staff to ensure that full participation and inclusion are an integral part of the culture of the institution.*

ASSISTANT PROFESSOR
of Biological Sciences

The Smith College Department of Biological Sciences invites applications for a tenure-track Assistant Professorship in terrestrial plant physiological ecology beginning July 1, 2011. A Ph.D. is required; teaching and/or postdoctoral experience is preferred. For more information and to apply, visit **website: http://jobs.smith.edu.** Review of applications will begin on November 8, 2010. *Smith College is an Equal Opportunity Employer encouraging excellence through diversity.*

Okinawa Institute of Science and Technology
New Faculty Positions in Physics

The Okinawa Institute of Science and Technology (**OIST http:// www.oist.jp**) invites applications for new faculty positions as it enters a period of growth in preparation for transition to an international graduate university in 2012. Approximately 15 faculty positions in several areas will be filled during this search. OIST provides a world-class research environment in newly completed facilities in an area of distinctive culture, unique ecology, and outstanding natural beauty.

Prof. Jonathan Dorfan, an internationally recognized experimental physicist, has been selected as the President of the graduate university. As the former Director of SLAC at Stanford, he has extensive experience supporting research in particle physics and the broad range of physical, chemical and life sciences that form the diverse program of the X-ray science carried out at SLAC's synchrotron source and its new X-ray laser.

The current OIST program is strongly focused in the Life Sciences and includes genomics, developmental biology, mathematical and computational biology, molecular & cell sciences and neuroscience. There is also a growing program in environmental science particular in the area of marine science. The present search seeks to establish the foundations of a complementary program focused in the physical sciences with several new appointments. We seek experimentalists and theorists in sub-disciplines including, but not limited to: hard and soft condensed matter physics; atomic, molecular and optical science; physics of biological systems; material science, nanomaterials; nanostructures; quantum computation; quantum coherence; membranes; single molecule spectroscopy; structural molecular biology, computational physics, and fluid mechanics.

The nature of the physical plant and the non-departmental academic structure of OIST are specifically designed to foster inter- and cross-disciplinary research, thus facilitating research in new areas that could stimulate and enhance the existing areas of focus. Applicants with exceptional skills in the development of novel research tools and instrumentation, particularly approaches that will further revolutionize visualization and labeling and/or the manipulation of bio- and nano-systems and/or single molecule or atom probes, are strongly encouraged to apply.

Successful candidates will be given the opportunity to excel in their chosen area of research, and will be expected to contribute to graduate teaching, research supervision and other academic activities. Applicants should have a PhD or equivalent degree, and demonstrate excellence in research.

The initial appointment will be as Principal Investigator (PI) or Independent New Investigator (INI) for a term of five years. When the transition to a graduate university is completed in 2012, it is planned that PI and INI positions will change to a tenure track system with Assistant Professors, Associate Professors, and Professors. Some appointments will be made on a joint or part-time basis. Substantial internal funding will be provided to support the faculty member's research based on a 5-year research plan that is renewable after scientific review.

At a time when worldwide support for research is increasingly risk-averse and obtaining funding places an ever-growing burden on faculty, OIST promotes innovative research in a highly facilitating and supportive environment. This is achievable because OIST has internal research funding, offers outstanding central research facilities, and consults faculty on the design of new laboratory space. Central research facilities at OIST include core facilities for high performance computing, mass spectrometry, X-ray crystallography, confocal microscopy, radioisotope use, electron microscopy, sequencing and genomic analysis, genetic recombination facilities, and vivarium.

OIST is committed to being international with more than 50% of faculty, researchers, and students from outside Japan. The official language of OIST is English. OIST is an equal opportunity, affirmative action employer and encourages applications from women.

More details regarding the aims of the search and advantages of working at OIST are available in the Information for Applicants in the application package that is downloadable from the website (**http://www.oist.jp/en/newsevent/careers/542-faculty-positions.html**). Applications should be submitted in accordance with the instructions in the application package. Applications for the current search close **8 October 2010**. Interviews will take place in late October/November, with a view to making appointments early in 2011.

Chair and Chief, Department of Pediatrics

Yale School of Medicine
Yale-New Haven Hospital

Applications are invited for the position of Chair of the Department of Pediatrics at Yale University School of Medicine and Chief of Pediatrics at Yale-New Haven Hospital. Candidates will have an outstanding academic record in research, clinical care and education, will be experienced administratively with the interpersonal skills for multidisciplinary communication, will have exceptional leadership talent, and are expected to meet the requirements for appointment to the senior faculty ranks.

Applicants should send a curriculum vitae, brief statement of interest, and a list of professional references prior to **November 15, 2010**, electronically to **Kathleen.Heath@yale.edu** or by mail to: **Brian R. Smith, MD; Chair, Pediatric Search Committee, c/o Kathleen Heath, Dean's Office, Yale School of Medicine, 333 Cedar Street, I-202 SHM, PO Box 208049, New Haven, CT 06520-8049**.

Yale University is an Equal Opportunity, Affirmative Action Employer and values diversity among its employees. Women and minority group members are encouraged to apply.

Dartmouth-Hitchcock NORRIS COTTON CANCER CENTER

Faculty Position
Tumor Immunology and Immunotherapy
Dartmouth Medical School

The Department of Microbiology and Immunology in collaboration with Norris Cotton Cancer Center (NCCC) at Dartmouth Medical School and Dartmouth-Hitchcock Medical Center seeks candidates for a full-time tenure-track or tenured faculty position at the rank of Associate or Full Professor. We offer the opportunity to join a dynamic group of outstanding basic and translational scientists with a broad range of expertise in cellular and molecular immunology, in addition to Dartmouth's collaborative community of internationally recognized investigators. The successful candidate will be an established immunologist with expertise in the broadly defined area of tumor immunology and immunotherapy and strengths in specific areas such as (but not limited to) immunotherapy, tumor vaccines, innate immunity, tumor microenvironment, and pathogen-induced tumors. Candidates with an interest in translational approaches are particularly encouraged to apply. Candidates should have a PhD, DVM, and/or MD degree(s), an outstanding academic record, and an externally funded research program. The investigator will have access to excellent students from an interdepartmental graduate program and will be expected to participate in teaching and mentoring at the graduate and postgraduate levels. The candidate will be eligible for additional support from the Immunology Program through an NIH-sponsored T32 training grant for graduate students and postdoctoral researchers and a Center of Biomedical Research Excellence (COBRE) grant.

The laboratories at Dartmouth are state-of-the-art and well equipped. Norris Cotton Cancer Center is an NCI-designated comprehensive cancer center that supports innovative cancer research through pilot projects, interdisciplinary programs, outstanding core facilities, and regulatory and administrative assistance. A full range of shared research core facilities, including flow cytometry and cell imaging, genomics, bioinformatics, transgenics and animal imaging, and pathology are available to all investigators in the Dartmouth community. Dartmouth Medical School has fully integrated patient care, medical education, and research activities. Additional information is available on the websites for the Microbiology and Immunology department and the Cancer Center websites: **http://dms.dartmouth.edu/microbio/** and **http://www.cancer.dartmouth.edu/**.

Applicants should submit, in electronic PDF format, a curriculum vitae, statement of research interests and accomplishments, record of extramural grant support, and contact information, including email addresses for at least three references to: **tumorimmunology@dartmouth.edu**. Review of applications will begin immediately and will continue until the position is filled.

Dartmouth is an Affirmative Action/Equal Opportunity Employer. Women and members of minority groups are strongly encouraged to apply.

POSITIONS OPEN

STANFORD SCHOOL OF MEDICINE
Stanford University Medical Center

FACULTY POSITION
Department of Biochemistry
Stanford University School of Medicine

Applications or nominations are invited for an **ASSISTANT PROFESSOR** position in the Department of Biochemistry. Applicants should have an established record of excellence in original research. The principal criterion for appointment in the University tenure line is a major commitment to research and teaching. Candidates should submit in one complete document, curriculum vitae including a list of publications; a description of their research interests; and names, addresses, telephone numbers, and e-mail addresses of three references to **e-mail: biochemistry_recruitment@stanford.edu.** Applications should be received by October 15, 2010. Reference letters should be sent to the above e-mail address or to: **Search Committee Chair, Department of Biochemistry, Stanford University School of Medicine, 279 Campus Drive Room B400, Stanford, CA 94305-5307.**

Stanford University is an Equal Opportunity Employer and is committed to increasing the diversity of its faculty. It welcomes nominations of and applications from women and members of minority groups, as well as others who would bring additional dimensions to the University's research, teaching and clinical missions.

ASSISTANT PROFESSOR
Chemical Biology
Utah State University

The College of Science at Utah State University invites applications for a tenure-track position at the Assistant Professor level in the area of Chemical Biology beginning fall 2011. Individuals whose research involves the use of chemical techniques to address important biological problems are strongly encouraged to apply. The position will be attached to either the Department of Chemistry and Biochemistry or the Department of Biology within the College of Science, affiliation to be determined by the qualifications of the successful candidate. Applicants must have earned a Ph.D. in Chemistry, Biochemistry, Biology, or a related field; postdoctoral experience is required. The position requires the development of an externally funded research program as well as teaching at the undergraduate and graduate levels. Applicants should submit curriculum vitae, a concise description of future research projects and associated major research infrastructure needs, a statement of teaching philosophy, and the names and e-mail addresses of three references. Apply online at **website: http://jobs.usu.edu** (Req ID **052265**). Evaluation of applicants will begin October 30; posting will remain open until position is filled.

Utah State University is an Equal Opportunity/Affirmative Action Employer committed to assembling a diverse faculty. Women and members of minority groups are strongly encouraged to apply.

The Harvard University Department of Psychology invites applications for a tenure-track **ASSISTANT PROFESSOR** position in the area of Clinical Psychology, to begin July 2011. Applicants must have an active, high-quality research program with potential for extramural funding and an ability to contribute to the undergraduate and doctoral teaching missions of the department, including the American Psychological Association-accredited doctoral program in clinical science. Those whose research uses approaches from cognitive and affective neuroscience, molecular genetics, and epigenetics to answer questions about mood disorders or other forms of psychopathology are especially encouraged to apply, although all competitive applications will be considered. Please submit your application by the October 15, 2010 deadline. Applications should be sent to: **Chair, Clinical Psychology Search Committee, Harvard University, 33 Kirkland Street, Cambridge MA 02138,** and should include curriculum vitae, selected reprints/preprints, a research and teaching statement, and three letters of recommendation. *Women and minority candidates are strongly encouraged to apply. Harvard University is an Equal Opportunity/Affirmative Action Employer.*

POSITIONS OPEN

DUKE GENOME SCIENCES & POLICY

TENURE-TRACK FACULTY POSITIONS
in Computational Biology
Duke University

The Department of Biostatistics & Bioinformatics (B&B) and the Institute for Genome Sciences & Policy (IGSP) at Duke University are seeking candidates for tenure-track or tenured faculty positions at the **ASSISTANT, ASSOCIATE,** or **FULL PROFESSOR** level. Candidates are expected to have a Ph.D. or equivalent degree in a quantitative discipline (computational or systems biology, statistics, computer science, engineering, physics or similar). We invite applications from researchers with an established track record in developing and applying computational approaches to cutting-edge problems in genomics and genetics, with a demonstrated interest in collaborative research.

Successful candidates will have their academic home in the Department of Biostatistics & Bioinformatics and will be Investigators in the cross-campus IGSP, which is home to several established research initiatives, including systems biology, genomic medicine, and regulatory and evolutionary genomics. Secondary appointments or affiliations may be arranged in other departments or centers, as appropriate. The collaborative nature of these positions will provide successful candidates with access to exceptional resources, including substantial cluster computing infrastructure, multiple next generation sequencing platforms, a diverse set of large biomedical datasets and multidisciplinary partnerships. Candidates will be expected to participate actively in the educational programs of both B&B and IGSP, as well as teach and mentor students in the cross-departmental graduate program in Computational Biology and Bioinformatics.

Interested applicants should submit application materials (cover letter, curriculum vitae, and a statement of research accomplishments and interests) and ask three references to submit reference letters at **website: http://www.academicjobsonline.com.** Further inquiries may be directed to **Kim Hall** at **e-mail: kim.hall@duke.edu.** Applications received by October 31, 2010 will be given full consideration.

Additional information may be obtained from our **websites: http://www.genome.duke.edu, http://www.biostat.duke.edu, http://www.genome.duke.edu/CBB.**

Duke University is an Affirmative Action/Equal Opportunity Employer. Women and minorities are encouraged to apply.

TENURE-TRACK ASSISTANT PROFESSOR
Synthetic Organic or Bioorganic Chemistry
Indiana University, Bloomington

The Department of Chemistry at Indiana University invites applications for a tenure-track faculty position at the Assistant Professor level in organic or bioorganic chemistry beginning August 2011. A Ph.D. in chemistry or a related field is required and postdoctoral experience is preferred. Successful candidates will be expected to develop a visible, externally funded research program, teach at the graduate and undergraduate level, and participate in a new graduate training program in Quantitative and Chemical Biology at Indiana University. We seek applicants with interests in exploring biomimetic approaches and/or in the development and application of emerging technologies toward the total synthesis of bioactive natural products. Applicants should send a complete curriculum vitae and a summary of future research plans and arrange to have four letters of recommendation forwarded to the Department. Applications completed by November 1, 2010, will receive full consideration, but review will continue until the position is filled. Applications and recommendation letters should be addressed to: **Professor David R. Williams, Chair, Faculty Search Committee, Department of Chemistry, Indiana University, 800 E. Kirkwood Avenue, Bloomington, IN 47405** or sent as PDF files electronically to **e-mail: chemchair@indiana.edu.** *Indiana University is an Affirmative Action/Equal Opportunity Employer and especially encourages applications from women and members of minority groups.*

POSITIONS OPEN

Ohio State Medical Center

The Department of Neuroscience at the Ohio State University plans to hire several tenure-track **NEUROSCIENTISTS** beginning this academic year. The Neurosciences Signature Program, which also comprises Neurology and Neurological Surgery, has been targeted for significant investment at the Ohio State University Medical Center. Although we are interested in applicants who demonstrate an exceptional record of research accomplishment in basic neuroscience, we are particularly interested in individuals whose research interests build on current or emerging strengths in spinal cord and brain injury, neurophysiology, neuroendocrinology, and mechanisms of neural degeneration/regeneration and who provide translational links to our clinical colleagues. State-of-the-art research facilities are available. Applicants should submit curriculum vitae, a statement of research interests, and three letters of reference to: **Randy J. Nelson, Department of Neuroscience, Ohio State University, Columbus, OH 43210.** Application materials may be submitted electronically (preferably in PDF format) to **e-mail: cheryl.yoder@osumc.edu.** Application deadline: 15 November 2010. *The Ohio State University has a strong commitment to diversity and actively encourages applications from candidates from individuals of underrepresented groups. The Ohio State University is an Equal Opportunity/Affirmative Action Employer.*

The Harvard University Department of Psychology anticipates making a tenure-track appointment at the **ASSISTANT PROFESSOR** level, to begin July 1, 2011.

We seek candidates with exceptional promise in the social psychology of emotion. Research and teaching expertise might include topics such as social psychophysiology, nonverbal communication of emotion, social embodiment, emotion contagion, or empathy; quantitative methodological expertise is also desirable. Our interest is less in specific areas than in innovation and excellence.

Candidates should expect to have completed the requirements for the Ph.D. prior to appointment and to have demonstrated a promise of excellence in both research and teaching. Teaching duties will include offerings at both undergraduate and graduate levels.

Candidates should submit curriculum vitae and representative reprints, and have at least three letters of recommendation sent to: **Social Emotion Search Committee, Harvard University, Department of Psychology, William James Hall 230, 33 Kirkland Street, Cambridge, MA 02138.** The closing date for applying is October 1.

Applications from women and minority groups are strongly encouraged. Harvard University is an Affirmative Action/Equal Opportunity Employer.

RESEARCH FACULTY POSITIONS
Department of Dermatology
Duke University School of Medicine

The Department of Dermatology, Duke University School of Medicine, is seeking applicants for research faculty positions. Applicants with interest in the molecular mechanisms of skin cancer, malignant melanoma, or in the study of inflammation and autoimmunity are encouraged to apply. Candidates should have M.D., M.D.-Ph.D., or Ph.D. degree and postdoctoral research experience to document significant accomplishment and future success. Academic rank and compensation will be based on the qualifications of the successful applicants.

Interested candidates should submit a letter of application, curriculum vitae, and the names of three references to:

Russell P Hall, III M.D.
J. Lamar Callaway Professor and Chair
Department of Dermatology
Box 31 35
Duke University School of Medicine
Durham, NC 27710

Applications will be accepted via **e-mail: vkb1@notes.duke.edu.** *Duke is committed to achieving excellence through diversity. Duke University is an Equal Opportunity/Affirmative Action Employer.*

Cell and Systems Biology – University of Toronto

The Department of Cell and Systems Biology at the University of Toronto invites applications for a tenure track faculty position to be appointed at the level of Assistant or Associate Professor beginning July 1, 2011.

We are interested in outstanding candidates that complement existing strengths in the department in the areas of genomics, plant and microbial biology, cell and developmental biology, and neurosciences using high-throughput approaches or gene/protein network analyses with genomic, proteomic, or advanced cell biological and imaging tools. We will consider all outstanding applicants within the framework of the Department of Cell and Systems Biology. For more information, please visit our home page at **http://www.csb.utoronto.ca/**.

Candidates should have at least two years of research experience beyond their doctoral degree. In addition to pursuing a vigorous, internationally-recognized research program, the successful candidate will contribute to undergraduate and graduate teaching in the molecular life sciences. The successful candidate would also be expected to network with researchers across the university to take advantage of the extensive resources in cell and systems biology at the University of Toronto and its affiliated institutions. A generous start-up package will be provided. Salary will be commensurate with qualifications and experience.

Qualified candidates must submit their applications online at: **www.jobs.utoronto.ca/faculty.htm**. Applicants should submit a single pdf file (<2Mb) that includes a cover letter, their curriculum vitae, and statements of research and teaching interests. Applicants should also arrange for at least three confidential letters of recommendation to be sent directly to: **Professor Ulrich Tepass, Chair, Department of Cell and Systems Biology, University of Toronto, 25 Harbord Street, Toronto, Ontario M5S 3G5, Canada**; or by email to **csbsearch@utoronto.ca** by **October 24, 2010**.

The University of Toronto is strongly committed to diversity within its community and especially welcomes applications from visible minority group members, women, Aboriginal persons, persons with disabilities, members of sexual minority groups, and others who may contribute to the further diversification of ideas. All qualified candidates are encouraged to apply; however, Canadians and permanent residents will be given priority.

Assistant/Associate Professor in the School of Biology

The Georgia Institute of Technology® is one of the top educational/research institutions in the country and ranked as one of the best places to work. As part of aggressive growth in the biological sciences, the School of Biology is seeking applications for two faculty positions at the Assistant/Associate Professor level. One position is in **Macromolecular Assemblies**, with particular interest in using mammalian cell, small animal or microbial models for studying pathogenic or functional self-assembled protein complexes. Another position will be in **Integrative Genomics**, using some combination of genomics, transcriptomics, proteomics and metabolomics to elucidate the quantitative genetic basis of variation for complex traits in animal (including human) and/or microbial models. These new faculty will be invited to join the Center for Nanobiology of the Macromolecular Assembly Disorders (NanoMAD) and/or Center for Integrative Genomics, respectively. Candidates also will be favored who integrate well with the department's existing strengths in molecular and cell biology, ecology and evolutionary biology, and computational biology (www.biology.gatech.edu). Georgia Tech® is an interdisciplinary environment where biologists are encouraged to interact with faculty from other areas of science, engineering and computing. It is therefore not uncommon for biology faculty to have joint or adjunct appointments in other departments.

Candidates should forward a letter of application specifically highlighting Macromolecular Assembly and/or Genomics, full curriculum vitae, statement of research interests and plans, and contact information for four references to **faculty@biology.gatech.edu.** Review of applications begins October 15, 2010.

Georgia Tech is a unit of the University System of Georgia and an Affirmative Action/Equal Opportunity Employer and requires compliance with Immigration Control Reform Act of 1986.

The Helen L. and Martin S. Kimmel Center for Stem Cell Biology at the Skirball Institute of Biomolecular Medicine

NYU Langone Medical Center

FACULTY POSITIONS

The Helen L. and Martin S. Kimmel Center for Stem Cell Biology at the Skirball Institute of Biomolecular Medicine at New York University Langone Medical Center invite applications for tenure-track positions at the assistant, associate or full professor level. We seek applicants with an exceptional record of achievement to join the Kimmel Center for Stem Cell Biology and the Skirball Institute faculties. The Stem Cell Center and the Skirball Institute are highly interdisciplinary, and combine research strengths at NYU Langone Medical Center and the College of Arts and Sciences. Special priority will be given to applicants who use mammalian stem cell systems.

The NYU Langone Medical Center offers excellent resources to support new faculty, including generous start-up packages and core facilities for siRNA screening, cell sorting, imaging, proteomics, mouse molecular genetics, genomics and structural biology. Successful candidates are expected to initiate and maintain vigorous independent research programs that will enrich and be enriched by the highly collaborative environment at the Skirball Institute and throughout the NYU research community. This is an electronic application process only.

Please create your application packet by formatting it as a single PDF document. Use the following page order: 1) Cover Letter; 2) Curriculum Vitae; 3) Research Statement; 4) One Recent Publication.

Email the application packet to stemcellsearch@med.nyu.edu by November 1st, 2010. Three letters of reference should be sent independently to stemcellsearch@med.nyu.edu.

New York University was founded in 1841 and is an equal opportunity affirmative action employer. Women and minority candidates are encouraged to apply.

Kimmel Center for Stem Cell Biology
www.med.nyu.edu/kimmelcenter

Skirball Institute of Biomolecular Medicine
http://skirball.med.nyu.edu

Science Careers online @sciencecareers.org
FACULTY POSITIONS

POSITIONS OPEN

ASSISTANT or ASSOCIATE PROFESSOR
Center of Excellence for Infectious Diseases

The newly created Center for Excellence in Infectious Diseases at the Paul L. Foster School of Medicine, Texas Tech University Health Sciences Center, El Paso, Texas is seeking candidates for tenure-track faculty positions at Assistant or Associate Professor level. This is part of a state-funded initiative to enhance research in infectious diseases. The Center is primarily interested in investigators with research interests in molecular immunology, host-pathogen interactions, vaccine development, and animal models for translational studies.

Successful candidates are expected to develop and maintain independently funded research programs in infectious diseases or a related field. The position reports to the Co-Directors of the Center of Excellence for Infectious Diseases.

Minimum Qualifications: M.D or Ph.D. degree in a related field and at least three years of postdoctoral experience with a strong publication record.

Preferred Qualifications: Candidates with funded grant support and experience in emerging infectious diseases and cutting edge technologies are particularly encouraged to apply.

The center offers competitive salary and startup packages, newly constructed laboratory space, BSL-2 and BSL-3 laboratories, and a supportive interactive environment. Interested candidates must apply online at **website: http://jobs.texastech.edu,** requisition **#81327** by submitting curriculum vitae, a short write-up of research interests, and three letters of recommendation. For further information, please electronically mail or contact:

Manjunath Swamy, M.D.
e-mail: manjunath.swamy@ttuhsc.edu or
Premlata Shankar, M.D.
e-mail: premlata.shankar@ttuhsc.edu
Co-Directors of the Center of Excellence for Infectious Diseases

The position is open until filled. Application review will begin immediately.

Texas Tech University Health Sciences Center is an Equal Opportunity/Affirmative Action Employer.

TENURE-TRACK BIOCHEMISTS
Brody School of Medicine

The Department of Biochemistry and Molecular Biology, Brody School of Medicine at East Carolina University (ECU) invites applications for two tenure-track **ASSISTANT PROFESSOR** positions (12-month appointments). We seek candidates with a Ph.D. degree in Biochemistry or related field and at least two years of postdoctoral training. Candidates should demonstrate a strong interest in medical and graduate education as well as excellence, originality and productivity in research. Development of a successful, externally funded research program is expected.

Preference will be given to candidates with basic science research expertise in two designated growth areas at Brody: (1) Obesity, diabetes, and cardiovascular disease, or (2) Oncogenesis and cancer metabolism. Candidates should submit online: curriculum vitae, a brief statement of research plans, and the contact information for three references at **website: http://www.jobs.ecu.edu.** Review of applications will begin November 1, 2010. Applications from individuals in underrepresented groups are encouraged.

Brody is one of two medical schools in the University of North Carolina system. Additional information can be found at: **website: http://www.ecu.edu/cs-dhs/biochemistry/.**

ECU is an Equal Opportunity/Affirmative Action University that accommodates individuals with disabilities. Individuals requesting a disability accommodation under the Americans with Disabilities Act (ADA) should contact the Department for Disability Support Services at 252-737-1016 (Voice/TTY). Proper documentation of identity and employability is required at the time of employment.

POSITIONS OPEN

UNIT LEADER
FISHERY BIOLOGIST
Alaska Cooperative Fish and Wildlife Research Unit, Fairbanks, Alaska

This is a Federal position with the U.S. Geological Survey (USGS) in the Alaska Cooperative Fish and Wildlife Research Unit within the Institute of Arctic Biology, University of Alaska Fairbanks. The Cooperative Fish and Wildlife Research Unit Program was established to facilitate cooperation between the Department of the Interior, universities, State natural resource agencies, and the Wildlife Management Institute, and to conduct research and graduate education related to ecosystems, and fish, wildlife, and their habitats. Unit scientists have graduate faculty appointments at their host institution, serving without salary compensation from the University. Responsibilities: Plans, conducts, and directs research related to freshwater fish biology or ecology, population dynamics and management; develops a substantial working relationship with state and federal natural resource agencies; supervises Federal research scientists and assists with career development; prepares scientific reports for publication in journals and for presentation to scientific and conservation organizations; acts as a major advisor to graduate students; and teaches one graduate level course per year in the area of his/her expertise. A Ph.D. in fishery biology or directly related field of study is required for this position.

For more information about the Alaska Cooperative Fish and Wildlife Research Unit, please see **website: http://www.akcfwru.uaf.edu/.**

Job applications must be submitted electronically through USAJOBS (**website: http://www.USAJobs.opm.gov**). For more information, please refer to vacancy announcement numbers: **WR-2010-0519** and **WR-2010-0520.** Please note the section on "Who May Be Considered" in the announcements. Both announcements will run concurrently for one Unit Leader position to be filled at either the GS-13 or GS-14 level. Applications will be accepted until October 15, 2010.

The Federal Government is an Equal Opportunity Employer.

ASSISTANT PROFESSOR
Evolutionary Biology
Occidental College, Los Angeles CA

The Department of Biology invites applications for a tenure-track position beginning August 2011. The successful candidate will have a research program in bird evolution, systematics, and/or biogeography as well as curatorial experience and the ability to combine teaching and specimen-based research in the Moore Laboratory of Zoology at Occidental, a collection of over 60,000 birds primarily from Mexico, Central America, and California. Preference will be given to candidates who can provide leadership in the management of Moore Lab and its integration into our curriculum. Teaching duties will include introductory biology, advanced courses in the area of specialty, and core courses in the college curriculum. Occidental is a nationally ranked liberal arts college with excellent research and teaching facilities, located near Caltech, other research institutions, and the varied habitats of southern California. The college is recognized for its diverse student body and its outstanding undergraduate research program. For more information on Occidental College and the position, please visit **website: http://college.oxy.edu/biology.** Inquiries should be addressed to: **Dr. Dan Pondella, Chair, Evolutionary Biology Search, e-mail: pondella@oxy.edu.** Review of applications will begin September 30, 2010 and continue until the position is filled. *Occidental College is committed to Affirmative Action; women and minority candidates are strongly encouraged to apply.*

POSITIONS OPEN

FACULTY POSITION
in Biophysics and Biochemistry

The Department of Biochemistry and Biophysics and the UNC Lineberger Comprehensive Cancer Center at UNC Chapel Hill (UNC-CH) invite applications for tenure and tenure-track faculty positions at the level of **ASSISTANT PROFESSOR** (other levels also considered). Candidates with cancer-related research and expertise in enzymology, redox biochemistry, chemical biology, computational biology, nanomedicine, signaling network analysis, systems biology, single molecule approaches, cryo-EM, and solid state NMR are especially encouraged to apply, but all areas of expertise in biophysics will be considered. UNC-CH provides an outstanding environment for interdisciplinary biomedical research with opportunities to interface with basic biological, physical, chemical, computational, and clinical scientists. Research strengths within the Department include, but are not limited to, computational biology, chromatin biology, DNA repair, cell signaling, cell adhesion, enzymology, membrane biophysics, virology, and structural biology. The UNC Center for Drug Discovery also actively works with faculty interested in converting biological and chemical insights into new therapeutics. Candidates should have a Ph.D. and/or M.D., postdoctoral research experience, and an outstanding publication record. Applications are reviewed until positions are filled. Women and members of underrepresented minority groups are especially encouraged to apply. Please visit **website: http://hr.unc.edu/careers-at-carolina/open-positions** to submit an online application and reference Recruit ID **#1000907.** Questions on this recruitment can be directed to **Amanda Chang** at **e-mail: ahc@med.unc.edu.**

University of North Carolina is an Equal Opportunity Employer.

EUKARYOTIC CELL BIOLOGIST
Biology

Tenure-track **ASSISTANT PROFESSOR** beginning August 2011 in the Biology Department at Colorado College. Specialization open, but we have particular interest in candidates who use some combination of genetics, molecular biology, biochemistry, bioinformatics, genomics, or microscopy as tools applied to model systems such as eukaryotic microbes (fungi, protozoa) or other organisms appropriate for undergraduates at a liberal arts college (e.g. zebrafish, Drosophila, or C. elegans). Preference will be given to candidates whose expertise complements existing faculty. Responsibilities include (1) teaching introductory, intermediate, and advanced courses for a new cell and molecular biology track; (2) teaching one or more courses appropriate for non-biology majors; and (3) development of a peer-reviewed research program involving undergraduates. Ph.D. and demonstrated excellence in undergraduate teaching required; postdoctoral experience highly desirable. Colorado College is committed to increasing the diversity of its community and curriculum. Candidates are encouraged to identify the ways in which they can contribute to that goal. Application deadline is September 30, 2010. Send letter of application, curriculum vitae, copies of graduate and undergraduate transcripts, statements of teaching philosophy and research interests, along with three letters of reference to: **Search Committee, Department of Biology, Colorado College, 14 East Cache la Poudre Street, Colorado Springs, CO 80903.** Colorado College is a highly selective liberal arts college with a unique one-course-at-a-time curriculum. *The College is an Equal Opportunity Employer that does not discriminate on the basis of race, color, age, religion, gender, sexual orientation, national origin, or disability in its educational programs, activities, or employment practices.*

ETH
Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Professor / Assistant Professor (Tenure Track) of Neuro-Electronics

The Department of Information Technology and Electrical Engineering (www.ee.ethz.ch) at ETH Zurich invites applications for a professorship or assistant professorship (tenure track) in Neuro-Electronics. The successful candidate is expected to develop a strong and visible research program in Biomedical Engineering. Research topics include electrically controlled biosystems, electrical neuroengineering, peripheral nerve and brain-machine interfaces, as well as artificial sight and hearing.

Candidates should have a Ph.D. degree and an excellent track record in Biomedical Engineering, Biophysics, Bioengineering, or related disciplines. In addition, commitment to teaching and the ability to lead a research group are expected. The new colleague will be expected to teach undergraduate level courses (German or English) and graduate level courses (English).

Assistant professorships have been established to promote the careers of younger scientists. The initial appointment is for four years with the possibility of renewal for an additional two-year period and promotion to a permanent position.

Please submit your application together with a curriculum vitae, a list of publications, and statements on future teaching and research activities **to the President of ETH Zurich, Prof. Dr. Ralph Eichler, ETH Zurich, Raemistrasse 101, 8092 Zurich, Switzerland (or via e-mail as one single pdf to faculty-recruiting@sl.ethz.ch), no later than October 31, 2010**. With a view toward increasing the number of female professors, ETH Zurich specifically encourages qualified female candidates to apply.

UMASS AMHERST

Department of Biology
Two Tenure-Track Assistant Professor Positions:
(1) Cellular Biophysics (2) Developmental Genetics

The Biology Department (www.bio.umass.edu/biology) at the University of Massachusetts Amherst invites applications for two tenure-track Assistant Professor positions to start as soon as September 1, 2011. One position is in the area of **Cellular Biophysics** and the other is in the area of **Developmental Genetics**. We seek individuals with outstanding research, a strong commitment to teaching, and the potential to develop and maintain an extramurally funded research program. The Biology Department provides an interactive and broad research environment, with faculty research spanning all levels of biological organization. Especially strong research clusters focus on nervous system development, cell biology, plant biology, functional morphology, and evolution. A Ph.D. and postdoctoral experience are required. Evaluation of applications for both positions will begin on **October 5, 2010** and continue until the positions are filled. Positions will be filled contingent upon University funding.

(1) **Cellular Biophysics position:** We seek a biologist who employs biophysical techniques to study cellular or tissue function. Research areas might include, but are not limited to, the biophysical properties and function of excitable cells. Optogenetic and imaging approaches to the study of neurobiology are of particular interest. The successful candidate will have a primary appointment in the Biology Department and be part of a growing biophysics cluster that includes research groups in the Physics, Biochemistry and Molecular Biology, and Chemistry Departments. **Application materials should include a curriculum vitae, research plan, teaching statement, and 3 letters of recommendation. Paper applications can be sent to: Biophysics Search #R39907, Biology Department, Attn: Sally Ives, 611 North Pleasant Street, University of Massachusetts, Amherst, MA 01003. Alternatively, application materials may be sent via email to: BiophysicsSearch@bio.umass.edu**

(2) **Developmental Genetics position:** We seek a biologist who works in the area of Developmental Genetics. Work with model systems, including nematodes, flies, or fish is particularly encouraged. **Application materials should include a curriculum vitae, research plan, teaching statement, and 3 letters of recommendation. Paper applications can be sent to: Developmental Genetics Search #R39908, Biology Department, Attn: Sally Ives, 611 North Pleasant Street, University of Massachusetts, Amherst, MA 01003. Alternatively, application materials may be sent via email to: DevGenSearch@bio.umass.edu**

New faculty members have the opportunity to participate in strong graduate training programs in Neuroscience and Behavior (www.umass.edu/neuro), Molecular and Cellular Biology (www.bio.umass.edu/mcb), Plant Biology (www.bio.umass.edu/plantbio), and Organismic and Evolutionary Biology (www.bio.umass.edu/oeb).

The University is part of the Five-College Consortium (www.fivecolleges.edu) in the Pioneer Valley in western Massachusetts, two hours from Boston and three hours from New York City. The University provides an intellectual environment committed to providing academic excellence and diversity including mentoring programs for faculty. The College of Natural Sciences and the Department of Biology are committed to increasing the diversity of the faculty, student body, and the curriculum.We strongly encourage women and members of minority groups to apply. The University of Massachusetts is an Affirmative Action/Equal Opportunity Employer.

OMRF

Discoveries That Make A Difference

Faculty Position in Free Radical Biology and Aging

The Oklahoma Medical Research Foundation (OMRF, **www.omrf.org**) is seeking an established investigator to join the Free Radical Biology and Aging Research Program. The area of research is open but individuals with expertise in animal model systems and biochemical approaches that complement the Program's general scientific theme in mitochondrial and metabolic regulation are especially encouraged to apply. Successful candidates will receive an appointment at the Associate or Full Member level (Associate and Full Professor equivalents) in the Program.

The Free Radical Biology and Aging Research program underwent major reorganization and renovation in 2008. Disease related areas of investigation focus on the role of free radicals in various musculoskeletal, neurological, metabolic, and cardiovascular disorders associated with the aging process and exacerbated by obesity and diabetes. Facilities in the program include substantial lab space for each investigator and shared spaces for cell culture, freezers, and animal procedures. Major new equipment in the program includes two LC-tandem mass spectrometry systems, equipment for metabolite analysis, an electron spin resonance instrument, and a small animal metabolic screening system. OMRF also supports a state-of-the-art AAALAC accredited animal facility and a small animal MRI and MRS core facility. Additional information can be found at our Program's website (**www.omrf.org/FRBA**). Other attractive aspects include a generous startup package, institutional support for competitive salaries, comprehensive benefits, and a collegial work environment. Overall, OMRF is committed to creating an attractive position suitable for an applicant with a proven track record of high quality funded research.

OMRF is an independent, not-for-profit, biomedical research institute that houses 50 independent research laboratories organized into 10 interdisciplinary research programs. Our facilities are located adjacent to the campus of the University of Oklahoma Health Sciences Center (OUHSC) in Oklahoma City. OMRF investigators enjoy close scientific interactions with OUHSC faculty and participate in OUHSC graduate programs. OMRF is in the early stages of a significant expansion that will increase the total number of principal investigators to approximately 75. This expansion includes the construction of a new eight-story research tower that is scheduled to open in early 2011.

Candidates should submit complete curriculum vitae and brief statement of research interests via e-mail to: **omrfcareers-mk@omrf.org**. Preliminary, confidential inquiries may be addressed to **Michael Kinter, Ph.D., Chair, FRBA Search Committee, mike-kinter@omrf.org**.

EOE/AA

POSITIONS OPEN

Drexel University College of Medicine

FACULTY POSITION
Chemical Approaches to Biological Problems

The Department of Biochemistry & Molecular Biology at the Drexel University College of Medicine invites applications for a tenure-track faculty position at the **ASSISTANT** or **ASSOCIATE PROFESSOR** level. We seek interactive individuals who are working at the interface of chemistry and biology, using chemical and/or structural approaches to tackle important problems in biology and medicine. Areas of particular interest include protein structure and function, inhibitor and drug design, mechanistic enzymology, metalloproteins, and metabolism. Individuals whose research complements existing strengths in the department (**website: http://www.drexel.edu/med/biochemistry**) are especially encouraged to apply. The Department is conveniently located in Center City, Philadelphia, and offers a collegial and stimulating environment with many opportunities for collaboration. Competitive startup funds are available. Successful candidates will have a Ph.D. and/or M.D., relevant postdoctoral experience, and a strong record of research accomplishments. Faculty are expected to establish vigorous, independent, and well-funded research programs and to participate in graduate and medical education.

The Drexel University College of Medicine is the nation's largest private medical school. Drexel University is ranked among the top 100 universities in the nation, and has recently been named as one of the top "Up-and-Coming" national universities in the 2011 U.S. News College Rankings.

To apply, please submit a single PDF containing curriculum vitae, statement of research interests, statement of teaching philosophy, and names of three references to **e-mail: lucia.boyer@drexelmed.edu;** please include the words "Chemical Biology Search" on the subject line.

FACULTY POSITION
in Systems Neuroscience
Department of Biological Sciences
Carnegie Mellon University

The Department of Biological Sciences and the Center for the Neural Basis of Cognition (CNBC) at Carnegie Mellon University seek to fill a tenure-track position in systems neuroscience at the **ASSISTANT PROFESSOR** level. Preference will be given to individuals using imaging or electrophysiological methods to examine the dynamic properties of neurons in vivo, or high throughput methods to evaluate genetic determinants of animal behavior in health and disease states. Carnegie Mellon is strongly committed to expanding brain research spanning multiple disciplines, investing significantly in new faculty in computational, cognitive, and systems neuroscience and in new facilities, including a state-of-the-art animal facility, high-performance computing clusters, and new neuroimaging centers (see **websites: http://www.cmu.edu/bio** and **http://www.cnbc.cmu.edu**).

The candidate will join a growing and highly interactive neuroscience community at Carnegie Mellon and will be a member of the CNBC, an interdisciplinary and collaborative group of neuroscientists from Carnegie Mellon and the University of Pittsburgh (including the University of Pittsburgh Center for Neuroscience and the University of Pittsburgh School of Medicine).

Carnegie Mellon offers highly competitive salaries and startup packages in an attractive urban environment. Interested candidates should submit curriculum vitae, research and teaching statements, reprints, and three letters of recommendation to **website: https://apps.bio.cmu.edu/facultySearch/view/4.** Questions can be directed to **Dr. Alison Barth,** Chair of the search committee.

Review of applications will begin October 1, 2010, and will continue until the position is filled. *Carnegie Mellon University is an Equal Opportunity/Affirmative Action Employer.*

POSITIONS OPEN

FOUR FACULTY POSITIONS
in Chemistry
Department of Chemistry
University of North Carolina at Chapel Hill

The Department of Chemistry at the University of North Carolina at Chapel Hill invites applications for four tenure-track faculty positions at the **ASSISTANT PROFESSOR** level. Areas of interest include inorganic chemistry, physical chemistry, material science, and energy science. However, all areas of chemistry, broadly defined, will be considered. Successful candidates are expected to develop an exceptional research program and to teach at both the graduate and undergraduate levels.

Applications will only be accepted electronically. Applicants should submit a single PDF containing a cover letter, curriculum vita, research plan, and teaching statement, and up to three reprints or preprints to: **website: http://jobs.unc.edu/2500420.** Applicants should also arrange to have four PDF letters of recommendation sent electronically to **e-mail: chemsearch@unc.edu.**

Applicants must indicate the focus of their research in the "major/expertise" field at **website: http://www.jobs.unc.edu/2500420** by using one of the following keywords: analytical, biological, inorganic, organic, physical, polymer/materials. Review of applications will begin October 18, 2010, and will continue until positions are filled.

Questions should be directed to: **Chair, Faculty Search Committee, Department of Chemistry, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599-3290. E-mail: chemsearch@unc.edu.**

UNC is an Equal Opportunity/Affirmative Action Employer, and strongly encourages applications from women and minorities.

FACULTY POSITION
in Genomic and Systems Biology
Department of Biological Sciences
Carnegie Mellon University

The Department of Biological Sciences at Carnegie Mellon University seeks to fill a tenure-track position in genomic and/or systems biology at the **ASSISTANT PROFESSOR** level. Outstanding candidates working on a broad range of problems within these fields will be considered. Areas of interest include, but are not limited to: genome organization, diversity and function, regulatory networks and pathways, and systems-level approaches to cellular and developmental processes. Research programs of current faculty include the areas of genetics and molecular biology, cell and developmental biology, biochemistry and biophysics, computational biology, and neuroscience (see **website: http://www.cmu.edu/bio**).

Carnegie Mellon fosters interdisciplinary research and outstanding opportunities exist for collaborations with faculty in the Ray and Stephanie Lane Center for Computational Biology, the Molecular Biosensor and Imaging Center, the Center for Nucleic Acids Science and Technology, computer science, bioengineering, robotics, and other departments. Successful candidates will be expected to develop a strong, innovative research program and to participate in the undergraduate and graduate educational programs. Candidates must have a doctoral degree and extensive research experience.

Carnegie Mellon offers highly competitive salaries and startup packages in an attractive urban environment. Interested candidates should submit curriculum vitae, research and teaching statements, reprints, and three letters of recommendation to **website: https://apps.bio.cmu.edu/facultySearch/view/5.**

Review of applications will begin October 1, 2010, and will continue until the position is filled. Questions can be directed to **Dr. Javier Lopez,** Chair of the search committee. *Carnegie Mellon University is an Equal Opportunity/Affirmative Action Employer.*

POSITIONS OPEN

Yale

RESEARCH ASSOCIATE
in Live Cell Imaging, Yale Medical School

Position available for **POSTDOCTORAL** Research Associate with experience in cell culture and live cell imaging to join multidisciplinary research team at Yale Medical School studying pathophysiology of axonal diseases and channelopathies. Ph.D. and/or M.D. degree and publications in cell culture and live cell imaging are essential. Experience with neuronal cell culture and ion-sensitive or membrane potential-sensitive imaging or neurodegeneration assays are highly desirable. Superb opportunity to interact with highly collaborative team of molecular and cell biologists, electrophysiologists, pharmacologists, etc. Send curriculum vitae, statement of interest and three letters of reference to: **Stephen G. Waxman, M.D., Ph.D., Director, Center for Neuroscience and Regeneration Research, Yale University School of Medicine**. **E-mail: stephen.waxman@yale.edu.**

Equal Opportunity/Affirmative Action Employer.

ASSISTANT PROFESSOR

The Department of Chemistry and Biochemistry at Denison University invites applications for a tenure-track position at the Assistant Professor level, starting fall 2011. Area of specialization is open. A Ph.D. is required; successful candidates will demonstrate a strong commitment to teaching at the undergraduate level, show the capacity to develop a productive research program that involves undergraduates, and complement the range of course and research opportunities currently available to our students. Teaching responsibilities will include courses in our core curriculum and advanced courses in the candidate's field of expertise. Denison University is a selective and nationally ranked residential liberal arts college located in Granville, Ohio, 30 minutes east of Columbus. We have well-developed programs in both chemistry and biochemistry and a broad range of instrumentation that is used in both teaching and research. See our **website: www.denison.edu/chemistry** for more detailed descriptions of the position and our program. Applicants should submit a cover letter addressing their motivations for teaching at a residential, liberal arts college, a statement of teaching philosophy, a statement indicating how they will foster a classroom and research environment that engages students from diverse backgrounds and contribute to the diversity of our department and college, a summary of research plans, curriculum vitae including a publication list, and undergraduate and graduate transcripts. These materials and contact information for three references should be submitted online at **website: https://employment.denison.edu.** To assure full consideration, completed applications must be received by October 1, 2010. *Our college is committed to attracting and supporting an academically and culturally diverse faculty.*

INORGANIC CHEMISTRY FACULTY POSITION

California Institute of Technology invites applications for a tenure-track faculty position in the Division of Chemistry and Chemical Engineering in the area of inorganic chemistry. Candidates with strong commitments to research and teaching excellence are encouraged to apply. We expect to make an appointment to an exceptionally well-qualified applicant at the **ASSISTANT PROFESSOR** level, but consideration may be given to outstanding applicants at the **ASSOCIATE** and **FULL PROFESSOR** levels. Appointment will be contingent upon completion of all requirements for a Ph.D. in chemistry or in a related field. Submit curriculum vita, publication list, a description of proposed research, and three letters of recommendation electronically to Chair of the Inorganic Search Committee at **e-mail: icsearch@caltech.edu.** Applications should be received by November 1, 2010. *The California Institute of Technology is an Equal Opportunity/Affirmative Action Employer. Women, minorities, veterans, and disabled persons are encouraged to apply.*

PENNSTATE
University Park

Plant Biology/Bioenergy Faculty Position

The Department of Biology at The Pennsylvania State University invites applications for a tenure-track faculty position at the **Assistant or Associate Professor level in Plant Biology**, with research at the molecular, cellular, genetic or systems level relevant to plant-based bioenergy. This includes fundamental research on plant cell walls, control of carbon allocation, and other topics of basic plant biology connected with energy storage and utilization. PSU is an international center for plant biology research, with an outstanding interdisciplinary plant biology graduate program (**http://www.huck.psu.edu/education/plant-biology**) and excellent core facilities, including bio-imaging, genomics, and proteomics. PSU is the lead institution for the Center for Lignocellulose Structure and Formation (**www.lignocellulose.org**), a DOE-funded Energy Frontiers Research Center, and applications relevant to this center are particularly encouraged. Prospective candidates should have a strong record of research accomplishments, and a commitment to teaching undergraduates. Interactions and collaborations with established research programs at PSU are strongly encouraged. E-mail letter of application, curriculum vitae, research prospectus, statement of teaching interests, and contact information of at least three references, all as a single PDF document, to **plantenergy104@bio.psu.edu**. Publications and manuscripts (not more than three) may also be submitted as separate PDF documents along with the application. Review of applications will begin **1 October, 2010**. *Penn State is committed to Affirmative Action, Equal Opportunity and the diversity of its workforce.*

OMRF

Discoveries That Make A Difference

Faculty Positions in Arthritis and Clinical Immunology

The Research Program of Arthritis and Clinical Immunology at the Oklahoma Medical Research Foundation (OMRF, **www.omrf.org**) seeks to understand roles of the immune system in health and disease. With a new expansion underway, we invite qualified candidates to apply for newly established research faculty positions. We are currently recruiting for Assistant or Associate Member level positions (Assistant or Associate Professor equivalents) but talented candidates at all levels are encouraged to apply and will be considered.

Successful candidates must have a PhD or MD/PhD in Immunology, Virology, or related field, and a strong record of scientific accomplishment. For one area of our research, we seek applicants interested in the interface between infection and immunity. Candidates with strong interests in Epstein-Barr virus or influenza are preferred. For another focus of our research, we seek applicants interested in autoimmune disease, especially systemic lupus erythematosus, rheumatoid arthritis, multiple sclerosis, or thrombotic thrombocytopenic purpura or animal models of those diseases. Successful candidates will be expected to maintain vigorous, independent research programs with associated external funding that directly address clinically relevant questions in their respective research fields.

Arthritis and Clinical Immunology investigators have access to a number of outstanding OMRF core facilities, including a Sample Procurement and Processing Core, Immunophenotyping Core, Clinical Core, Flow Cytometry Core and state-of-the-art clinical facilities. Extensive autoimmune disease and control sample collections are also available. Successful candidates will receive a generous, multi-year start-up package with significant, sustained salary and research support.

OMRF (**www.omrf.org**) is an independent, not-for-profit biomedical research institute adjacent to the campus of the University of Oklahoma Health Sciences Center (OUHSC) in Oklahoma City. OMRF investigators enjoy close scientific interactions with OUHSC faculty and participate in OUHSC graduate programs. For more information about Arthritis and Clinical Immunology, visit: **www.omrf.org/ACI**.

To apply, please send a CV, a concise future research plan, names and contact information for three professional references, and up to three recent publications to **Dr. Judith James** at **omrfcareers-jj@omrf.org**. Review of applications will begin immediately and continue until the position is filled. We offer attractive salaries, institutional support and comprehensive benefits.

EOE/AA

Western University

www.westernu.edu

Faculty Positions in Physiology available for 2011

College of Osteopathic Medicine of the Pacific – Northwest Lebanon, Oregon

Western University of Health Sciences, a thriving center for human health care and veterinary medicine education is opening a new site for the College of Osteopathic Medicine of the Pacific – Northwest (COMP-NW) in Lebanon, Oregon with the inaugural class beginning in Fall, 2011. The University's 10 year plan and core values have propelled the Institution to be a benchmark University for the development of interprofessional and graduate medical education. The University values a diverse institutional community and is committed to excellence in its faculty, staff and students. Western University seeks applicants of distinguished academic accomplishments who possess a passion for excellence and can illustrate a proven track record of achievements.

The Department of Basic Medical Sciences provides the preclinical education for the College of Osteopathic Medicine, and invites applications from highly motivated individuals for tenure-track faculty positions in physiology. These are full-time, 12-month, tenure-track positions at the Assistant Professor/Associate Professor/Professor rank dependent upon qualifications. Similar positions in pharmacology, biochemistry/genetics, and microbiology/immunology are also available at both the Lebanon, OR and Pomona, CA campuses. Successful candidates and faculty will be located at the new site on the COMP-NW campus. Applicants must have a Ph.D. in physiology or equivalent field and at least 2 years of postdoctoral experience. Preference will be given to master educators who have demonstrated excellence in teaching with significant scholarly activity and/or those with a history of extramural funding and a strong potential to obtain further grant support for their research program. Submit a current curriculum vitae and a cover letter describing your teaching experience and philosophy, your research activity and goals, and how you meet the qualifications for the position. Please include contact information for at least three references. These positions will remain open until filled.

Nissar A. Darmani, PhD
Assistant Dean for Basic Sciences and Research
Department of Basic Medical Sciences
College of Osteopathic Medicine of the Pacific
Western University of Health Sciences
309 E. Second Street, Pomona, CA 91766-1854
Email Address: ndarmani@westernu.edu
www.westernu.edu

Western University of Health Sciences is an equal opportunity employer.

Faculty Position
Cell Biology Program
Sloan-Kettering Institute

The Cell Biology Program, Sloan-Kettering Institute (www.ski.edu) has initiated a search for tenure-track faculty members. We are interested in outstanding individuals who have the potential to develop an innovative, independent research program that complements and enhances our existing strengths. Candidates with research interests in exciting areas of eukaryotic cell biology, including aspects of stem cell biology, and using a variety of experimental approaches and systems are encouraged to apply. New faculty will be eligible to hold graduate school appointments in the Gerstner Sloan-Kettering Graduate School of Biomedical Sciences, the Weill Graduate School of Medical Sciences of Cornell University, as well as the Tri-Institutional MD/PhD Training Program. Sloan-Kettering has an outstanding infrastructure as well as state-of-the-art core resources, and we are now significantly expanding our research programs.

The deadline for applications is November 1, 2010. Interested candidates should visit **http://facultysearch.ski.edu** to access the on-line faculty application. Please visit the site as soon as possible, as it contains important information regarding the required application materials, including deadlines for submission of letters of reference. Informal inquiries may be sent to **Tiffany Lennon at lennont@mskcc.org** or **Dr. Alan Hall, Chair, Cell Biology Program at halla@mskcc.org**. Memorial Sloan-Kettering Cancer Center is an equal opportunity and affirmative action employer committed to diversity and inclusion in all aspects of recruiting and employment. All qualified individuals are encouraged to apply.

Memorial Sloan-Kettering Cancer Center
www.mskcc.org

POSITIONS OPEN

FACULTY POSITIONS
in Chemosensory Research

The Monell Chemical Senses Center invites applications for full-time faculty positions. We seek outstanding investigators from diverse disciplines who are interested in pursuing clinical or basic research in the chemical senses and/or allied disciplines (e.g., neuroscience or nutrition) as they relate to the chemical senses. Candidates must possess a Ph.D. or M.D. and have postdoctoral experience. Prior experience in chemosensory research is not required. The successful candidate will be expected to develop and fund an independent research program and collaborate with colleagues at the Center. Both junior and senior level applicants are welcome. The Monell Center, founded in 1968, is the world's premier institute devoted to basic, multidisciplinary research on the mechanisms and function of olfaction, gustation, and chemesthesis. Further information about the Center can be found at **website: http://www.monell.org.**

Applicants should send the following materials in electronic form to **e-mail: hr0709pd@monell.org:** curriculum vitae, three representative publications, statement of research interests, and the names and addresses of three individuals willing to provide letters of reference. Review of applications will begin September 30th, 2010.

The Monell Center is an Equal Opportunity Employer and encourages applications by women and minorities.

ASSOCIATE PROFESSOR or PROFESSOR of Biomedical Science

The Charles E. Schmidt College of Medicine is seeking a tenure-track or tenured faculty member at the rank of Associate or Full Professor to teach microbiology to medical and graduate students. The applicant should have a well developed research program focusing on mechanisms and/or therapies of human diseases. The successful candidate will have Ph.D. and/or M.D.

Preferred candidates will have research interests that complement those of current faculty, a demonstrated ability to conduct innovative research, a strong record of external grant awards, and must be currently funded. The position includes startup funds and a 12 month salary.

Application materials must be submitted electronically including: cover letter, curriculum vitae, a one-page summary of research interests, a one-page statement of teaching experience and philosophy, and the names of three references to **website: https://jobs.fau.edu.** Reference the position number **981310** by October 31, 2010. Credentials will be subject to Florida Public Records Law. A background check is required for the candidate selected for this position. *Florida Atlantic University is an Equal Opportunity/Equal Access Institution. For accommodation, call 561-297-2216. For communication assistance, call 7-1-1.*

CHEMICAL BIOLOGY

The Department of Chemistry at the University of Michigan invites applications for a tenure-track position at any rank with a proposed start date of September 1, 2011. Candidates with research interests in the area of chemical biology will be given priority. This would be a University-year appointment (nine-month academic salary with summer salary supported by research funds). Candidates are expected to develop an internationally recognized program of scholarly research and to excel in teaching at undergraduate and graduate levels. Detailed information regarding the electronic application process and required materials is available online at **website: https://www.chem.lsa.umich.edu/chem/facultyrecruit/**. The position will remain open until filled but preference will be given to applicants who have submitted all requested materials prior to October 15, 2010. Information about the Chemistry Department is available on the **website: http://www.umich.edu/~michchem.** Questions about the application process should be sent to **e-mail: chemfac10@umich.edu.** *Women and minorities are encouraged to apply. The University of Michigan is supportive of the needs of dual career couples and is an Equal Opportunity/Affirmative Action Employer.*

LOYOLA MARYMOUNT UNIVERSITY
Frank R. Seaver College of Science and Engineering

Tenure-track **FACULTY POSITION** for **MARINE ECOLOGY:** The Department of Biology at Loyola Marymount University (LMU) invites applications at the rank of **ASSISTANT PROFESSOR** beginning fall 2011. The campus is situated on a bluff overlooking the Ballona Wetlands. It is within a day's drive or boat ride of beaches, deserts, mountains, the California Channel Islands, and Baja California. Individuals with a Ph.D. in Biology, Zoology, or related fields are encouraged to apply. The candidate is expected to teach lower division courses in general biology, field-based upper division courses in marine biology/intertidal ecology, and courses in his or her specialty area. In addition to excellent teaching of undergraduates, the candidate is expected to establish an active research program that will include undergraduate students. Applicants should be able to teach a diverse student body. Please send a letter of application, curriculum vitae, selected publications, a statement of teaching philosophy within an institution such as LMU, a description of research projects, and arrange for three letters of recommendation to be sent to: **Dr. Martin Ramirez, Department of Biology, Loyola Marymount University, 1 LMU Drive M.S. 8220, Los Angeles, CA 90045-2659.** Review of applications will commence 15 October 2010 and continue until the position is filled.

Tenure-track **FACULTY POSITION** for **CELL PHYSIOLOGY/BIOCHEMISTRY:** The Department of Biology at Loyola Marymount University invites applications at the rank of **ASSISTANT PROFESSOR** beginning fall 2011. Individuals with a Ph.D. in Biology, Biochemistry, or related field are encouraged to apply. The candidate is expected to teach lower division courses in Biology, upper division courses in Biochemistry, and courses in his or her specialty area. In addition to excellent teaching of undergraduates, the candidate is expected to establish an active research program that will include undergraduate students. LMU's Seaver College of Science and Engineering offers courses and conducts research in biochemistry, cell biology, molecular biology, genomics, and bioinformatics. Loyola Marymount, a comprehensive university in the mainstream of American Catholic higher education, seeks professionally outstanding applicants who value its mission and share its commitment to academic excellence, the education of the whole person, and the building of a just society. Applicants should be able to teach a diverse student body. Please send a letter of application, curriculum vitae, selected publications, a statement of teaching philosophy within an institution such as LMU, a description of research projects, and arrange for three letters of recommendation to be sent to: **Dr. Philippa Drennan, Department of Biology, Loyola Marymount University, 1 LMU Drive M.S. 8220, Los Angeles, CA 90045-2659.** Review of applications will commence 15 October 2010 and continue until the position is filled.

LMU is an Equal Opportunity Institution actively working to promote an intercultural learning community. Women and minorities are encouraged to apply.

The University of Rochester Department of Chemistry invites applications in the area of Inorganic Chemistry, broadly defined. This search is primarily for candidates at the **JUNIOR** level, but exceptional **SENIOR CANDIDATES** can also be considered. Candidates are expected to establish an outstanding program of original research, and be effective teachers at the graduate and undergraduate levels. Application materials are to be submitted online at **website: https://www2.chem.rochester.edu/facultyapp/.** Materials submitted are to include curriculum vitae indicating graduate and postdoctoral advisors, a statement of research plans, and a statement of teaching interests. Junior candidates will be instructed how to arrange for three letters of recommendation to be submitted electronically. The Department will solicit letters for senior candidates. Review of completed applications will begin on October 4, 2010. *The University of Rochester has a strong commitment to diversity and actively encourages applications from candidates from groups underrepresented in higher education. The University is an Equal Opportunity Employer.*

ASSISTANT PROFESSOR
Biological Chemistry
The Johns Hopkins University School of Medicine

The Department of Biological Chemistry at The Johns Hopkins University School of Medicine invites applications for a tenure-track faculty position at the Assistant Professor level. The Department is seeking candidates with an outstanding record in any area of biochemistry, cellular, or molecular biology and a commitment to excellence in research and teaching. Applicants should submit (preferably as a single PDF file) curriculum vitae, a list of publications and a summary of research and future plans by November 15, 2010. Electronic files should be sent to **e-mail: bcrecruit@jhmi.edu.** Applicants should also request that three letters of recommendation be sent electronically or to the address below:

Craig Montell, Ph.D.
Committee Chair
C/O Ms. Claire Brzeczko
Department of Biological Chemistry
The Johns Hopkins University
School of Medicine
725 North Wolfe Street
Baltimore, M.D. 21205-2185

Equal Opportunity/Affirmative Action Employer.

FACULTY POSITIONS
MIT Department of Chemistry

The Massachusetts Institute of Technology (MIT) Department of Chemistry invites applications for tenure-track appointments beginning July 2011. Outstanding applicants with teaching and research interests in all areas of chemistry are encouraged to apply. MIT Chemistry has particular interest in appointments in the areas of Organic and Biological Chemistry, broadly defined. Applicants working at the interface of these and related areas are also sought. Appointments will be at the rank of **ASSISTANT PROFESSOR,** but outstanding senior applicants may be considered. A completed application will include curriculum vitae, a one-page summary of research plans, two or more research proposals, a brief statement of teaching interests, and three or more letters of recommendation.

Applications are being accepted at Academic Jobs Online at **website: https://academicjobsonline.org/ajo.**

To receive full consideration, completed applications must be received by October 4, 2010.

Search Contact: **Ms. Karen Fosher, Personnel Administrator, Department of Chemistry, Room 18-392, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, MA 02139-4307.** (**E-mail: kfosher@mit.edu**).

MIT is an Equal Opportunity/Affirmative Action Employer. Applications from women, minorities, veterans, older workers, and individuals with disabilities are strongly encouraged.

ASSISTANT PROFESSOR of CHEMISTRY

The Department of Chemistry of the University of Chicago invites applications from outstanding individuals for the position Assistant Professor of Chemistry. This search is in the areas broadly defined as inorganic, organic, and physical chemistry. Applicants must apply online to the University of Chicago Academic Career page at **website: http://tinyurl.com/36pmntk.** Applicants must upload a cover letter, curriculum vitae with a list of publications, and a succinct outline of research plans. The cover letter should be addressed to the **Inorganic Search Committee, Organic Search Committee,** or **Physical Search Committee,** depending on the discipline of interest. The successful candidate must have a Ph.D. in Chemistry or related field. In addition, three reference letters will be required. Review of completed applications will begin October 1, 2010. To ensure full consideration, all material should be submitted by that date.

The University of Chicago is an Affirmative Action/Equal Opportunity Employer.

MASSACHUSETTS GENERAL HOSPITAL
HARVARD STEM CELL INSTITUTE

The **Center for Regenerative Medicine (CRM)** at Massachusetts General Hospital invites applications for a tenure-track Assistant Professor position. Outstanding scientists in the field of vertebrate stem cell or regenerative biology will be considered. Candidates with a research program focused on adult stem cell biology, tissue regeneration, pluripotency, neuroscience, or organ biology and who have an interest in application to human disease are especially welcome. Successful candidate(s) will be members of the **Harvard Stem Cell Institute** and faculty of **Harvard University**. Candidates must hold a PhD and/or MD and have a history of innovative, interactive research.

Applicants should send an electronic copy of (1) letter of interest (2) research plan and (3) current curriculum vitae to Miklosik.Mona@mgh.harvard.edu. Three letters of recommendation should also be sent directly to: **Center for Regenerative Medicine Search Committee, Attention: Mona Miklosik, Massachusetts General Hospital, 185 Cambridge St., CPZN 4258, Boston, MA 02114**.

Women and minority candidates are urged to apply. MGH is an Equal Opportunity/ Affirmative Action Employer.

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER
Paul L. Foster School of Medicine

Founding Director, Center of Excellence in Diabetes and Obesity

The Paul L. Foster School of Medicine at Texas Tech University Health Sciences Center in El Paso is seeking candidates for clinician-scientists or scientists to become the founding Director of the Center of Excellence in Diabetes and Obesity.

The Center of Excellence for Diabetes and Obesity is a newly created center established to promote excellence in basic and clinical sciences research, patient care, and education in health issues related to diabetes and obesity. Uniquely situated in a predominantly Hispanic population, the Center is expected to develop research in the areas of population genomics, clinical science and interventions intended to reduce the burden of complications in the population.

The founding Center Director will assemble an interdisciplinary team of investigators and demonstrate a clear vision of leadership including opportunities for translational research collaborations with the clinical departments. The successful candidate will be a recognized leader in diabetes-related research with a history of solid NIH funding and interdisciplinary collaborative research and will possess academic credentials for faculty appointment as a full professor.

The city of El Paso is nestled between the beautiful Franklin Mountains and the Rio Grande with over 300 days of sunshine a year. Ranked as the 2nd Safest City in America with a population of more than 500,000, the community offers a vibrant city life at an affordable cost of living, with excellent collaboration opportunities with the University of Texas at El Paso and William Beaumont Army Medical Center.

A competitive salary, comprehensive benefits package, and newly constructed lab space are available. Interested candidates may apply online at **http://jobs.texastech.edu**, requisition # 80443, by attaching a statement of research interests and a curriculum vitae or emailing them to:
Charles C. Miller, III, Ph.D.
Associate Dean for Research and Search Committee Chair
c/o Laura Duffy, Senior Associate, Korn/Ferry International
laura.duffy@kornferry.com

The position is open until filled. Application review will begin immediately.

Texas Tech University Health Sciences Center is an Equal Opportunity/Affirmative Action Employer.

JOHNS HOPKINS MEDICINE
SCHOOL OF MEDICINE

Faculty Positions in Physiology

The Department of Physiology seeks outstanding individuals with creative, rigorous and integrative research approaches to key physiological processes. Suitable candidates must have a Ph.D. and/or an M.D. degree; have exceptional promise and a proven record of research achievements. Presently, the Department's research interests include the physiology, and biophysics of membranes and membrane transport, computational biology, and the development and analysis of genetic diseases and metabolism. Our philosophy is to integrate the growing body of information on molecular and cellular processes into functionally relevant contexts that translate into important medical advances. Therefore, we are especially interested in individuals who relate the properties of individual proteins both to organ function and pathogenesis. Individuals who use genetic, computational or other models to study integrative physiology are encouraged to apply. Successful candidates will complement the research activities within the Institute for Basic Biomedical Sciences (see **http://www.hopkinsmedicine.org/ibbs/index.html**) and will actively participate in the graduate programs in Cellular and Molecular Physiology and in Biochemistry, Cellular and Molecular Biology as well as medical education. Further information about the Physiology Department is available at **http://physiology.bs.jhmi.edu/**.

Applicants will be assessed on an ongoing basis, with higher priority given to those who apply by **October 30, 2010**. The deadline to submit applications is **November 30, 2010**. Applicants must provide one electronic (PDF) document that includes a curriculum vitae, statement of research plans, copies of relevant publications and three to five letters of recommendation to: **physiologyrecruitment@jhmi.edu**, subject line **"Faculty position in Physiology."**

The Johns Hopkins University School of Medicine is an Affirmative Action/Equal Opportunity Employer that embraces diversity.

Research Faculty
Computational and Systems Biology

The Computational Biology Program (http://cbio.mskcc.org) at MSKCC (mskcc.org) seeks innovative investigators for tenure-track positions at the Assistant, Associate, or Full Professor level. Pursue basic research, solve biological problems with major emphasis on computational methods, and build active bridges to experimental and clinical research. Actively participate in building out research programs at one of the best clinical-scientific institutions in the world. Work in MSKCC's new Zuckerman Research Center, on Manhattan's Upper East Side, in close proximity to Rockefeller University and the Cornell Weill Medical College. Train graduate students in the Gerstner Sloan-Kettering Graduate School (sloankettering.edu), the Weill Cornell Graduate School of Medical Sciences and in tri¬institutional graduate programs.

Areas of special interest include **chemical biology, physiology, developmental biology, neurobiology, genetics and cancer biology.** Applicants should have a doctoral-level degree and the potential to develop an independent, interdisciplinary research program. MSKCC offers a highly interactive, supportive and dynamic research environment with programs in Computational Biology, Developmental Biology, Molecular Pharmacology & Chemistry, Cancer Biology & Genetics, Structural Biology, Immunology, Cell Biology, Molecular Biology, and Human Oncology and Pathogenesis, as well as unparalleled clinical programs in cancer research, treatment and prevention.

The deadline for applications is **November 1, 2010**. Please visit **www.cbio.mskcc.org/faculty-search** for specific application instructions including the required IMPACT format of your bibliography. To access the on-line faculty application, go to **http://facultysearch.ski.edu**. Please visit the site as soon as possible, as it contains important information on the required application materials, including deadlines for submission of letters of reference. Inquiries may be sent to **Chris Sander, Chair, Computational Biology Program via Dwana Agosto, Program Coordinator, at agostod@mskcc.org**. MSKCC is an equal opportunity and affirmative action employer committed to diversity and inclusion in all aspects of recruiting and employment. All qualified individuals are encouraged to apply.

Memorial Sloan-Kettering Cancer Center
www.mskcc.org

POSITIONS OPEN

JUNIOR or SENIOR FACULTY POSITIONS in the Environment
Yale School of Forestry & Environmental Studies

The Yale School of Forestry & Environmental Studies seeks up to three exceptional Natural, Physical, or Social **SCIENTISTS** to diversify and/or strengthen the current teaching and research portfolio of a strongly interdisciplinary School. The openings are available at both the tenure-track junior level and at the senior level. Ideal candidates will have an outstanding record of original scholarship and will also demonstrate potential for collaborating with natural, physical, and social scientists within the School and more broadly at Yale, to address environmental issues of societal importance, such as the science, policy, and management of forest and freshwater resources, biodiversity, agriculture and land use, urbanization, and air pollution. Applications from candidates with strengths in environmental economics, the conservation and management of tropical forests, or holistic approaches to energy systems, will be particularly welcome. Successful candidates will be expected to develop an internationally recognized research program that involves graduate students, to work across disciplinary boundaries in a collegial environment, and to teach in both the Yale School of Forestry and Environmental Studies and in Yale College.

Applicants should submit curriculum vitae, a statement of research and teaching interests, and the names of four references via electronic mail to **e-mail: fesdeansoffice@yale.edu** or via surface mail to:

Environment Faculty Searches
c/o Pilar Montalvo, Dean's Office
Yale School of Forestry & Environmental Studies
195 Prospect Street
New Haven, CT 06511
USA

Prior to applying, candidates should explore the School's **website: http://www.environment.yale.edu** and consider how their expertise can strengthen or complement the strengths of the existing faculty of the School.

Applications received by October 29, 2010 will receive full consideration. For more information about the position, contact assistant dean **Pilar Montalvo** at **e-mail: pilar.montalvo@yale.edu.**

Yale University is an Affirmative Action/Equal Opportunity Employer. Men and women of diverse racial/ethnic backgrounds and cultures are encouraged to apply.

ORGANIC CHEMISTRY
Dartmouth College

Applications are invited for a tenured **ASSOCIATE** or **FULL PROFESSOR** faculty position starting July, 2011. The Chemistry Department seeks an individual who has already established a nationally recognized research program in synthetic organic chemistry with biochemical and/or medicinal applications, whose research interests will complement those of the current faculty, and who will excel at teaching in our undergraduate and Ph.D. curriculum. Chemistry with biological or medical applications is one of two targeted areas in the department's long-range plans. We particularly seek candidates who will help lead collaborative research projects both within Chemistry and involving other Dartmouth researchers, including those at Dartmouth's Medical School, Norris Cotton Cancer Center, and Thayer School of Engineering. Candidates will be expected to teach introductory and advanced courses in organic chemistry, as well as graduate courses in their area of research. Applicants should submit curriculum vitae, a description of their current research funding and future plans, a statement of their teaching interests, and names of at least three references. All inquiries and applications will be treated confidentially. Application materials should be sent to: **Chair, Organic Chemist Search Committee, Department of Chemistry, 6128 Burke Laboratory, Dartmouth College, Hanover, NH 03755-3564.** The Committee will begin to consider completed applications on October 15. *With an even distribution of male and female students and over a quarter of the undergraduate student population members of minority groups, Dartmouth is committed to diversity and encourages applications from women and minorities. Dartmouth College is an Equal Opportunity and Affirmative Action Employer.*

POSITIONS OPEN

ASSISTANT PROFESSOR in Biological Mathematics
The College of William and Mary

The Department of Biology at The College of William and Mary invites applications for a tenure-track position at the level of Assistant Professor in Biological Mathematics beginning fall 2011. The successful candidate will develop a productive, externally funded research program in biological mathematics, broadly construed, that includes collaborations with both faculty and students in the Department of Biology and, potentially, the Program in Neuroscience. Collaboration with faculty in the Departments of Applied Science and Mathematics is also encouraged. Typical teaching duties will be one course per semester; the successful candidate will develop and teach a sophomore level course in mathematical biology suitable for Biology majors and an advanced course that incorporates student research projects. In addition, the successful candidate will help to develop quantitative elements for introductory and advanced Biology courses in collaboration with the instructors of such courses. The assignment to teach a particular course might be substituted partially or entirely by collaborative work with other faculty members to develop and integrate biological mathematics into courses from the introductory to advanced level. An interest in and ability to teach biostatistics is preferred, but this need not be the research focus of the successful candidate. A Ph.D. is required and postdoctoral experience is desirable. Applications should include curriculum vitae, a statement of current and future research interests, and a statement of teaching interests and experience and should be submitted electronically as a single PDF to **website: http://jobs.wm.edu.** The system will also prompt you for the names and e-mails of a minimum of three references familiar with your research and/or teaching who will be asked to provide a reference letter. Questions should be addressed to **Margaret Saha** (**e-mail: mssaha@wm.edu**). Review of applications will begin on November 1, 2010 and will continue until an appointment is made. *The College of William and Mary is an Equal Employment Opportunity/Affirmative Action Employer and is committed to improving diversity.*

TENURE-TRACK POSITION
College of the Holy Cross

The Department of Chemistry at the College of the Holy Cross seeks a **CHEMIST** for a full-time tenure-track position to begin August 2011. The primary teaching responsibility includes General Chemistry with laboratory and an intermediate course in either Analytical/Instrumental Chemistry or Biochemistry in alternate years. More information about the College, Department, discovery curriculum, research program, and the newly completed $65 million Integrated Science Complex can be found at **website: http://www.holycross.edu.** Candidates must demonstrate commitment to, and excellence in, undergraduate teaching as well as scholarly achievement. This position carries a 3-2 teaching load with a full-salary, one-semester research leave prior to tenure review and generous sabbatical and fellowship leaves for senior faculty. Please send a cover letter describing teaching and research interests, curriculum vitae, official undergraduate and graduate transcripts (Ph.D. required), three letters of recommendation, a statement on teaching philosophy (including specific course interests), and a description of research plans (including estimated start-up costs and how undergraduates will be involved) to: **Chemistry Search Committee, Department of Chemistry, College of the Holy Cross, Worcester, MA 01610.** Review of completed applications will be conducted as they are received until October 15, 2010.

The College of the Holy Cross is a highly selective Catholic liberal arts college in the Jesuit tradition. It enrolls about 2,700 students and is located in a medium sized city 45 miles west of Boston. Holy Cross belongs to the Colleges of Worcester Consortium (**website: http://www.cowc.org**) and the New England Higher Education Recruitment Consortium (**website: http://www.newenglandherc.org/home/index.cfm**). *The College is an Equal Opportunity Employer and complies with all Federal and Massachusetts laws concerning Equal Opportunity and Affirmative Action in the workplace.*

POSITIONS OPEN

ASSISTANT PROFESSOR
Behavioral Neuroscience, Psychology Department

The Psychology Department at Northeastern University in Boston, Massachusetts, invites applications for a tenure-track position in the area of behavioral neuroscience at the Assistant Professor level, to start in the fall of 2011. Applicants should have a doctorate in psychology, behavioral neuroscience, neurobiology, or related field, a strong record of publication, and strong potential for external research funding. Responsibilities will include teaching undergraduate and graduate courses and conducting an independent, externally funded research program. We seek a talented scientist who will develop a research program investigating the molecular mechanisms underlying social and affective behavior using animal models, with preference given to those applicants whose research program incorporates recent molecular advances in epigenetic, viral vector, and gene knock-out technology. To apply, visit Careers at Northeastern at **website: https://psoft.neu.edu/psc/neuhrprdpub/EMPLOYEE/HRMS/c/NEU_HR.NEU_JOBS.GBL.** Click on "Faculty Positions" and search for the current position under the College of Science. Application materials to be submitted online include a cover letter, curriculum vitae, research statement, teaching statement, and a list of three references. The applicant should ask each reference to submit a letter (as a PDF attachment) directly to **e-mail: psychneuroresearch@neu.edu.** Review of applications will begin immediately. For full consideration, all application materials, including the reference letters, should be submitted by November 1, 2010. *Northeastern University is an Equal Opportunity/Affirmative Action Educational Institution and Employer/Title IX University. Northeastern University particularly welcomes applications from minorities, women and persons with disabilities. Northeastern University is an E-Verify Employer.*

MOLECULAR BIOLOGIST
Assistant Professor of Biology

The Department of Biology and Geology at the University of South Carolina Aiken (**website: http://www.usca.edu/biogeo**) seeks applications for a full-time, tenure-track Assistant Professor who will use cellular and molecular approaches to study biological processes. Ph.D. required; postdoctoral experience preferred. Start date: August 2011. Primary teaching responsibilities include undergraduate courses in introductory biology, biochemistry and a specialty area. The successful candidate will also develop an active research program and mentor undergraduate research projects. The Department has a history of funded research and places high value on undergraduate research.

Apply online at **website: https://uscjobs.sc.edu/applicants/Central?quickFind=65196** and submit transcripts and three letters of reference to: **Dr. Bill Pirkle, Department of Biology and Geology, USC Aiken, 471 University Parkway, Aiken SC 29801.** Review of applications will begin November 1, 2010 and continue until position is filled. *USC Aiken seeks to attract and retain a diverse faculty consistent with its diverse student body and the diversity in the surrounding community. Women and minorities are encouraged to apply. USCA is an Affirmative Action/Equal Opportunity Employer.*

CONTINUING NON-TENURE-TRACK Position in Biology, Bryn Mawr College

The Department of Biology invites applications for a continuing non-tenure-track **FACULTY POSITION** (**website: http://www.brynmawr.edu/provost/**) to teach post-baccalaureate premedical students beginning July 1, 2011. The successful candidate is expected to develop an introductory biology sequence with a laboratory component that is appropriate for preparing post-baccalaureate students for health related professions. We are particularly interested in candidates who are broadly trained in the biological sciences and have training and/or interests in a medically relevant field. A doctorate and at least one year of relevant teaching experience or postdoctoral research experience are required. Submit curriculum vitae, a statement of teaching interests, and arrange for three letters of recommendation to be sent by November 15, 2010, to: **Chair, Biology CNTT Search, Department of Biology, Bryn Mawr College, 101 N. Merion Avenue, Bryn Mawr, PA 19010-2899.**

SOUTHWESTERN
THE UNIVERSITY OF TEXAS
SOUTHWESTERN MEDICAL CENTER
AT DALLAS

Assistant Professor in Human Genetics

The Center for Human Genetics (McDermott Center) at The University of Texas Southwestern Medical Center at Dallas invites applications for a tenure-track position of Assistant Professor. We are seeking individuals with innovative experimental research programs in human molecular genetics. Successful applicants will be expected to establish a vigorous independent research program and to teach students at the graduate level.

The individual should hold a graduate degree (MD, PhD or MD/PhD) and have completed a postdoctoral fellowship. The appointment will include a competitive salary, attractive start-up package, and excellent laboratory space in a dynamic research environment with access to genetic core facilities. The faculty member will have a joint appointment in a basic science or clinical department. Applicants should submit their curriculum vitae containing a summary of past accomplishments, a statement of future objectives, and three professional references to:

Dr. Helen H. Hobbs
Professor and Director
McDermott Center for Human Growth and Development
UT Southwestern Medical Center at Dallas
5323 Harry Hines Boulevard
Dallas, Texas 75390-8591

UTSW is an Equal Opportunity Employer. Women and Minorities are encouraged to apply.

UNIVERSITY OF UTAH
SCHOOL OF MEDICINE

Tenure-track Assistant and/or Associate Professor of Human Genetics

The Department of Human Genetics in the University of Utah School of Medicine (**http://genetics.utah.edu/**) is seeking outstanding applicants for a tenure-track position at the level of Assistant or Associate Professor. We encourage applications from scientists with interests in genetic approaches to complex disease, population/statistical genetics, computational biology, functional genomics, and animal models of human disease. Our department has a strong history in human genetics, genomics, and developmental genetics, and our faculty members collaborate closely with faculty in other basic science and clinical departments. Creative scientists with a record of achievement and commitment to excellence in both research and teaching are encouraged to apply. Successful candidates will receive a highly competitive startup package and enjoy a stimulating and supportive research environment.

Applicants should submit an electronic version of current CV, summary of research plans, relevant reprints and/or preprints, and three letters of reference to:

Dr. Lynn B. Jorde
Professor and Chair
c/o Natalie Johnson, njohnson@genetics.utah.edu

Application materials, including letters of reference, must be submitted by **November 1, 2010**.

The University of Utah is an Affirmative Action/Equal Opportunity Employer and does not discriminate based upon race, national origin, color, religion, sex, age, sexual orientation, gender identity/expression, disability, or status as a Protected Veteran. Upon request, reasonable accommodations in the application process will be provided to individuals with disabilities. To inquire about the University's nondiscrimination policy or to request disability accommodation, please contact: Director, Office of Equal Opportunity and Affirmative Action, 201 S. Presidents Circle, Rm 135, (801)581-8365. The University of Utah values candidates who have experience working in settings with students from diverse backgrounds, and possess a demonstrated commitment to improving access to higher education for historically underrepresented students.

Tenure Track Faculty Position: Cancer Pharmacology or Drug Discovery Sloan-Kettering Institute

Sloan-Kettering Institute is seeking an innovative individual, for a tenure-track position at the Assistant or Associate Member level with strong research accomplishments in biology, biochemistry or pharmacology, who wishes to address problems of relevance to cancer research or cancer drug discovery and development. Faculty will be eligible to hold graduate school appointments in the Gerstner Sloan-Kettering Graduate School of Biomedical Sciences, the Weill Graduate School of Medical Sciences of Cornell University, as well as the Tri-Institutional MD/PhD Training Program and Tri-Institutional Training Program in Chemical Biology.

MSKCC offers a unique and exciting research environment with programs in Immunology, Pharmacology, Chemistry, Molecular Biology, Computational Biology, Genetics, Cell Biology, Developmental Biology, Cellular Biochemistry and Structural Biology. The presence of world-renowned clinical programs in cancer research, treatment and prevention offers unique opportunities for creative collaboration.

Applicants should have a Ph.D. or MD degree, postdoctoral experience, and dedication to important problems at the interface of biology, biochemistry or chemistry as they relate to cancer pharmacology.

The deadline for applications is November 1, 2010. Interested candidates should visit **http://facultysearch.ski.edu** to access the on-line faculty application. Please visit the site as soon as possible, as it contains important information on the required application materials, including deadlines for submission of letters of reference. Inquiries may be sent to **Marie Aiello at aiellom@mskcc.org** or to **Dr. David Scheinberg, Chairman, Molecular Pharmacology and Chemistry Program at scheinbd@mskcc.org**.

MSKCC is an equal opportunity and affirmative action employer committed to diversity and inclusion in all aspects of recruiting and employment. All qualified individuals are encouraged to apply.

Memorial Sloan-Kettering Cancer Center
www.mskcc.org

UCDAVIS

Faculty Position in Biomedical Engineering

The Department of Biomedical Engineering at UC Davis invites applications for an Assistant Professor position with emphasis on stem cell bioengineering. The BME Department has 27 faculty members and is ranked 6th in the nation in annual research expenditures (NSF rankings). The Department has existing strengths in the areas of tissue engineering, cellular and molecular engineering, biomechanics, biomedical imaging, micro/nano systems, therapeutics, and computational/systems biology.

A research emphasis in the translational aspects of stem cell bioengineering is favored; however, other related areas in tissue engineering or regenerative medicine will also be considered, so long that an emphasis exists toward clinical translation. Successful candidates are expected to integrate and complement the existing research strengths within BME, the various stem cell efforts (e.g., the Institute of Regenerative Cures), the School of Medicine, and the School of Veterinary Medicine. Candidates should have a Ph.D. in Biomedical Engineering or a closely related field, and a commitment to excellence in teaching and service.

Interested candidates should submit all materials via the web-based online submission system (**www.bme.ucdavis.edu**). Required materials include a curriculum vitae, brief statements of research and teaching plans, and names and contact information for at least five evaluators who have agreed to write letters of reference. Inquiries can be directed to the chair of the search committee at **bme-chair@ucdavis.edu**. The deadline for full consideration is **November 30, 2010**, although applications will be accepted until the position is filled.

UC Davis is an Affirmative Action/Equal Employment Opportunity Employer and is dedicated to recruiting a diverse faculty community. We welcome all qualified applicants to apply, including women, minorities, individuals with disabilities, and veterans.

POSITIONS OPEN

FACULTY POSITION
in Quantitative Biology and Biophysics
University Of Michigan

Biophysics and the Department of Molecular, Cellular, and Developmental Biology in the College of Literature, Science, and the Arts at the University of Michigan solicit applications for an anticipated tenure-track faculty position at the **ASSISTANT PROFESSOR** level, but appointment at a more senior level is possible for applicants with an outstanding record of productivity.

Successful candidates will be expected to establish a vigorous, extramurally funded research program in quantitative biology and biophysics and to be involved in instruction of both undergraduate and graduate students. We are especially interested in quantitative experimental or theoretical work across the supramolecular and the multicellular scales that lead to fundamental insights into the physical principles that govern biological function. Information about our current research areas can be found at **websites: http://www.biop.lsa.umich.edu** and **http://www.mcdb.lsa.umich.edu.**

Applicants should submit the following materials electronically at **website: http://biop.lsa.umich.edu/faculty-search.aspx:** curriculum vitae; a brief statement of present and future research plans; a statement of teaching interests, philosophy, and evidence of teaching excellence for those who have teaching experience; copies of three recent publications; and the names of at least three references. The deadline for applications is October 15th, 2010.

Women and underrepresented minorities are encouraged to apply. The University of Michigan is supportive of the needs of dual career couples and is an Equal Opportunity/Affirmative Action Employer.

INTEGRATIVE SYSTEMS or CELLULAR BIOLOGIST
Tenure-Track Position

The Department of Biology at Trinity University invites applications for an Integrative Systems or Cellular Biologist whose expertise contributes to the field of neurobiology. The position is tenure-track at the rank of **ASSISTANT PROFESSOR** beginning August 2011. Candidates must possess a Ph.D. and postdoctoral experience is desirable. Successful candidates must demonstrate commitment to excellence in teaching undergraduates and have the potential to develop and sustain a quality research program that involves significant undergraduate participation. Responsibilities include teaching upper division courses in the areas of specialty, participation in the introductory curriculum, and academic advising. Additionally, the candidate will interact with our integrative neuroscience majors program. Applicants should send curriculum vitae, statement of teaching philosophy, summary of research interests, selected publications, and contact information of three references to: **Professor Jonathan King, Chair of Search Committee, Department of Biology, Trinity University, One Trinity Place, San Antonio, TX 78212.** Electronic applications are encouraged and should be sent to **e-mail: jonathan.king@trinity.edu.** For more information on the department see **website: http://www.trinity.edu/departments/biology/.** Application deadline is 22 October 2010. *Women and minority candidates are strongly encouraged to apply. Trinity University is an Equal Opportunity Employer.*

ASSISTANT PROFESSORS
Uintah Basin

Two tenure-track Assistant Professor positions at Utah State University (USU) at the USU-Uintah Basin Regional Campus. One position in Physiological Ecology in the Department of Biology, and one position in the Department of Chemistry and Biochemistry for a Chemist or a Biochemist who will teach general chemistry, organic, and biochemistry. These positions are 70 percent teaching, 25 percent research, and 5 percent service. Qualified applicants should apply online following guidelines posted under Job Opportunities at the USU Human Resources **website: http://wwwusu.edu/hr/htm/employment** where full responsibilities and qualifications are described. *Affirmative Action/Equal Opportunity Employer.*

TENURE-TRACK FACULTY POSITION
Molecular and Cellular Neuroscience
Biology Department
Williams College

The Biology Department at Williams College, a premier liberal arts college with a long-standing tradition of excellence in the sciences, invites applications for a tenure-track position at the rank of **ASSISTANT PROFESSOR,** to begin July 2011. We are seeking a **NEUROBIOLOGIST** with research interests in the molecular and cellular aspects of neuronal function. The successful applicant will teach introductory courses in cellular and molecular biology, intermediate- and upper-level courses in molecular and cellular neurobiology, and participate in the Neuroscience Program. Normally, faculty members teach one course and two laboratory sections (or the equivalent) each semester.

A research program that attracts extramural funding and involves talented undergraduates is expected, and start-up funds and internal funding for research are available. A Ph.D., postdoctoral experience, and a strong research record are required. We anticipate an appointment at the beginning assistant professor level, although a more senior appointment is possible under special circumstances. Applicants should submit curriculum vitae, brief statements of teaching and research interests, and arrange for three letters of recommendation to be sent by October 22, 2010, to: **e-mail: neuroresearch@williams.edu, care of Steven Swoap, Chair, Department of Biology, Williams College, Williamstown, MA 01267.**

Beyond meeting fully its legal obligations for nondiscrimination, Williams College is committed to building a diverse and inclusive community where members from all backgrounds can live, learn, and thrive.

OPEN FACULTY POSITION
Boston College Chemistry Department
http://www.bc.edu/chemistry

The Chemistry Department at Boston College invites applications for the position of **ASSISTANT PROFESSOR** of Organic Chemistry (broadly defined). This is a tenure-track position with a hire date in the fall of 2011. Applicants will be evaluated on their potential to establish a prominent, externally funded research program and to excel in teaching at both the graduate and undergraduate levels. Successful applicants will join a department of approximately 30 postdoctoral fellows, 125 doctoral students, 200 undergraduate chemistry and biochemistry majors, and an internationally recognized faculty. A Ph.D. in Chemistry, Biochemistry, or a related area and postdoctoral experience are required.

Applicants must: Submit a cover letter, curriculum vitae, summary of research plans (maximum of eight pages), and summary of research accomplishments (two pages)—in one transmission using PDF files—to **e-mail: chemsearch@bc.edu.**

Arrange to have three letters of reference in PDF format transmitted to **e-mail: chemsearch@bc.edu.** Original letters may be requested by the department. In your cover letter, please specify the names and contact information of your three references.

Submit all application materials electronically on or before 15 October 2010.

Boston College, a university of eight schools and colleges, is an Equal Opportunity Employer and supports Affirmative Action.

SPINTRONICS and QUANTUM COMPUTATION
1st São Paulo School of Advanced Science

The Institute of Physics of São Carlos (**website: http://www.ifsc.usp.br**) will host a School on Spintronics and Quantum Computation, in São Carlos, São Paulo, November 1–5, 2010, aimed at graduate students and young postdoctoral fellows. Lecturers include **Peter Gruenberg, Daniel Loss, Peter Zoller, Seigo Tarucha, Stuart Parkin, Michael Flatte?,** among others. We will accept about 100 participants (50 from abroad) and cover their travel expenses (restrictions may apply). This School is an initiative of FAPESP—the São Paulo Research Foundation. For details see **website: http://www.spin2010.ifsc.usp.br/.** Further inquiries: **Professor J. Carlos Egues** (**e-mail: egues@ifsc.usp.br**), Institute of Physics of São Carlos, University of São Paulo, São Carlos, Brazil.

TENURE-TRACK FACULTY POSITION
Departments of Chemistry
and Biochemistry and Biology
Utah Science, Technology
and Research (USTAR) Initiative
Utah State University

The USTAR initiative, along with the Departments of Chemistry and Biochemistry and Biology at Utah State University, invite applications for a tenure-track position at any rank. Candidates must have a Ph.D. in Biochemistry, Biology, or a related field, with faculty experience preferred. The successful applicant is expected to continue and expand a funded research program in some area of phototrophic microbes, and will be expected to teach at the graduate and undergraduate levels. Preference will be given to candidates with research programs that complement the USTAR Biofuels research program goals of developing phototrophic microbes as a feedstock for biofuels. The position is funded by a grant from the USTAR initiative, a statewide program that aims to promote commercialization of technologies at the state Universities. Applicants should submit curriculum vitae, a concise description of future research projects, associated major research infrastructure needs, and the names and e-mail addresses of three references online at **website: http://jobs.usu.edu** (Req ID **052021**). Evaluation of applications will begin October 15 and will continue until the position is filled. For further information please visit our **website: http://www.chem.usu.edu.** *Utah State University is an Equal Opportunity/Affirmative Action Employer committed to assembling a diverse faculty. Women and members of minority groups are strongly encouraged to apply.*

ENVIRONMENTAL BIOLOGY
Haverford College

Haverford College (**website: http://www.haverford.edu**) seeks outstanding candidates for a tenure-track appointment in Environmental Biology at the **ASSISTANT** or **ASSOCIATE PROFESSOR** level, to begin fall 2011. Applicants using molecular and/or computational approaches to study fundamental questions in ecology, biodiversity, and/or plant biology are encouraged to apply. The successful candidate will contribute to a vibrant curriculum in cell and molecular biology, participate in an interdisciplinary Environmental Studies program that engages colleagues at Bryn Mawr and Swarthmore Colleges, and establish a vigorous, externally funded research program involving undergraduate students. Postdoctoral experience required. Apply by submitting a single PDF file containing cover letter, curriculum vitae, and statements of research plans and teaching interests to **e-mail: hc-environbio@haverford.edu.** Three formal recommendations, submitted separately by referees, are also required and should be sent to: **Merleen Macdonald, Haverford College, 370 Lancaster Avenue, Haverford, PA 19041.** Review of completed applications begins October 1. Specific questions may be directed to **Karl Johnson**, Chair, Biology Department. **Telephone: 610-896-1306.** *Haverford is an Equal Opportunity/Affirmative Action Employer committed to excellence through diversity and strongly encourages applications and nominations of persons of color, women, and members of other underrepresented groups.*

ORGANIC CHEMISTRY
FACULTY POSITION

California Institute of Technology invites applications for a tenure-track faculty position in the Division of Chemistry and Chemical Engineering in the area of organic chemistry. Consideration will be given to exceptionally well-qualified applicants at the **ASSISTANT, ASSOCIATE** and **FULL PROFESSOR** levels. Appointment will be contingent upon completion of all requirements for a Ph.D. in chemistry or in a related field. Outstanding candidates who have strong commitments to research and teaching excellence are encouraged to apply. Submit by October 15, 2010, your curriculum vita, publication list, a concise description of proposed research, and three letters of recommendation to: **Chair, Organic Search Committee, M/C 164-30, California Institute of Technology, Pasadena CA 91125.** *The California Institute of Technology is an Equal Opportunity/Affirmative Action Employer. Women, minorities, veterans, and disabled persons are encouraged to apply.*

UNC
LINEBERGER COMPREHENSIVE CANCER CENTER
N.C. CANCER HOSPITAL

Basic/Translational Cancer Research Faculty Position

The UNC Lineberger Comprehensive Cancer Center, in collaboration with departments in the School of Medicine and across the entire University of North Carolina Chapel Hill, seeks outstanding candidates for faculty positions at all levels and at all ranks in basic and translational cancer research. This broad-based recruitment seeks outstanding scientists in a number of areas, including but not limited to: animal models, signal transduction, cancer genetics, bioinformatics, virology, drug development and target validation, epigenetics and gene expression, DNA damage and repair, cancer therapy, cancer immunology, inflammation and cancer, and stem cells. Applicants should have a strong record of recent accomplishments as a postdoctoral fellow or sustained productivity as an established faculty member. Appointment and rank in an academic department will be determined by the applicant's qualifications.

Applications will be reviewed beginning **December 1, 2010** and until the positions are filled. Applicants must submit curriculum vitae, a description of research plans and names of four references through the UNC Chapel Hill's web-based system: **jobs.unc.edu/2500310**. Please note that application may first require registration in the system and then application. PDF documents are preferred.

The University of North Carolina at Chapel Hill is an Equal Opportunity/ADA Employer. Women and minorities are encouraged to apply.

UHealth | University of Miami Miller School of Medicine

FACULTY POSITION MOLECULAR AND CELLULAR PHARMACOLOGY

The Department of Molecular and Cellular Pharmacology at the University of Miami Miller School of Medicine is seeking applications for a **TENURE-TRACK FACULTY POSITION** (rank open). Candidates must have a Ph.D. and/or M.D. degree and have an established record of research excellence. Applicants from all areas of molecular/cellular biology and biomedical research are welcome, but we are particularly interested in research relating to the cardiovascular system to complement existing research efforts in this field. Rank and salary will be commensurate with experience. Competitive laboratory space and start-up funds will be offered.

Applicants should send electronic copies of their CV, statement of current and future research interests and the names and addresses of three references to **ELalor@med.miami.edu** and hard copies to **Ms. Elba M. Lalor, Asst. to the Chairman, Department of Molecular and Cellular Pharmacology, University of Miami Miller School of Medicine, P.O. Box 016189, Miami, FL 33101**.

An Equal Opportunity/Affirmative Action Employer.

UK

ASSISTANT PROFESSORS OF BIOLOGY UNIVERSITY OF KENTUCKY

The Department of Biology at the University of Kentucky seeks two tenure-track Assistant Professors with research programs in neuroscience. Areas of particular interest include, but are not limited to, nervous system development and regeneration, structural and behavioral plasticity, sensory and motor systems, and comparative neurobiology. Preference will be given to candidates who can conceptualize problems in neuroscience across levels of biological organization, linking, for example, molecular mechanisms to the physiology and behavior of cells, tissues, or individuals. Responsibilities for the successful candidates include establishment of an independent research program that is supported by awards from extramural agencies and contribution to the teaching mission of the Biology Department. For more details on the department and the university, visit our website (**http://biology.uky.edu**) or contact **Dr. Vincent Cassone, Chair, Department of Biology**, **vincent.cassone@uky.edu** or **(859) 257-6766**.

Applicants should send a letter of application, a curriculum vitae, statements on teaching philosophy and experience, and a description of the applicant's research program electronically to **ukbiology@uky.edu**. Applicants should also arrange for three letters of recommendation in PDF format on official letterhead to be sent to the same electronic address. The review of applications will begin **November 1, 2010**.

The University of Kentucky is an Affirmative Action/Equal Opportunity University that values diversity and is located in an increasingly diverse geographical region. It is committed to becoming one of the top public institutions in the country. Women, persons with disabilities, and members of other underrepresented groups are encouraged to apply. The University also supports family-friendly policies.

The University of Texas at Austin

Cancer Molecular Biology Position

The Institute for Cellular and Molecular Biology

The Institute for Cellular and Molecular Biology, Alan Lambowitz, Director, invites applications for a tenure-track/tenured position in cancer molecular biology. Academic appointments at the level of Assistant, Associate, or Full Professor will be in the section of Molecular Genetics and Microbiology in the College of Natural Sciences. Candidates should have an outstanding record of research productivity and a research plan that utilizes molecular and biochemical approaches to address important problems in cancer biology. Areas of particular interest include but are not limited to DNA damage responses, genome instability, post-translational regulatory mechanisms, chromatin, and small regulatory RNAs.

Building on a strong existing faculty, the Institute has recruited more than 50 new faculty members over the past ten years. In addition to its highly interactive and interdisciplinary research environment, the Institute provides administrative and financial support for the Graduate Programs in Cell and Molecular Biology, Microbiology, and Biochemistry, and state-of-the art core facilities including DNA sequencing, mass spectrometry, electron and confocal microscopy, DNA microarrays, robotics, mouse genetic engineering and Next-Gen sequencing. An MD-PhD program with the UT Medical Branch and the new Dell Pediatrics Research Institute enhance the environment for basic Biomedical Research.

Austin is located in the Texas hill country and is widely recognized as one of America's most beautiful and livable cities.

Please send a single PDF file containing your curriculum vitae, summary of research interests and names of three references before November 1, 2010 to: **mgm_search@biosci.utexas.edu.** References may also send their letters directly to the same email address.

Homepages • http://www.icmb.utexas.edu • http://www.biosci.utexas.edu/MGM •

The University of Texas at Austin is an Equal Opportunity Employer.
Qualified women and minorities are encouraged to apply; a background check will be conducted on applicant selected.

FACULTY POSITIONS in SYSTEMS NEUROSCIENCE

The Brain and Behavior Discovery Institute (BBDI) at the Medical College of Georgia (MCG) is seeking six to eight faculty members who will be appointed as tenure-track Assistant Professor, tenured Associate Professor, or Full Professor. Candidates should have a PhD or MD degree with a strong record of research accomplishment, working in the area of primate or rodent systems neurophysiology, coupled with fMRI, optogenetics, or brain-machine-interface technologies. Faculty members are expected to establish or have creative, cutting edge research programs and participate in teaching medical and graduate students. MCG is a state supported academic medical center located in a historic city with outstanding recreational and lifestyle opportunities.

Consideration of candidates will begin **October 1, 2010** and will continue until the search has been successfully concluded. Please submit a CV, a statement of current and future research interests, and arrange 3 letters of recommendation to:

Joe Z. Tsien, Ph.D.
Neuroscience Faculty Search Committee
The Brain and Behavior Discovery Institute (BBDI)
School of Medicine
Medical College of Georgia
1120 15th Street, CL-3033
Augusta, GA 30912-4750
ATTN: Toni Goodly
lgoodly@mcg.edu

You are also required to complete an online application at **http://www.mcg.edu/facultyjobs/** (req #'s 4780, 4781, 4782, 4783, 4784, 4785, 4786, 4788.

EEO/AA/Equal Access Employer.

DUQUESNE UNIVERSITY

Biological Sciences Faculty

Duquesne University invites applications for a tenure-track position in the Department of Biological Sciences. The successful applicant is expected to develop a vigorous independent research program involving the study of molecular, cellular, and/or organismal processes in eukaryotes. Areas of interest include, but are not limited to, molecular biology, cell biology, development, immunology, and physiology.

The successful candidate will join an active department of 18 faculty with a commitment to combining externally funded research with excellence in teaching at both the graduate and undergraduate levels. Applicants must have post-doctoral experience, and are expected to mentor MS and PhD students. Preference will be given to candidates at the Assistant Professor level. However, more senior candidates may also be considered. Competitive salary and start-up packages are available. Additional information about the Department can be found at **http://www.duq.edu/biology**.

To apply, send a cover letter, CV, statements of research and teaching goals, and three letters of recommendation to Chair, Biology Faculty Search Committee, Department of Biological Sciences, 201 Mellon Hall, 600 Forbes Avenue, Pittsburgh, PA 15282. Review of applications will begin October 15, 2010. Please direct inquiries about the position to **biology@duq.edu**.

Duquesne University was founded in 1878 by its sponsoring religious community, the Congregation of the Holy Spirit. Duquesne University is Catholic in mission and ecumenical in spirit. Motivated by its Catholic identity, Duquesne values equality of opportunity both as an educational institution and as an employer.

Jefferson Medical College

Department of Orthopaedic Surgery and the Rothman Institute

Assistant/Associate/Full Professors, Basic Sciences

The **Department of Orthopaedic Surgery** is recruiting basic science faculty for tenure-track positions at the Assistant/Associate/Full Professor levels. We are especially interested in applicants whose research focus complements and extends the Department's strengths in osteoarthritis and intervertebral disc disease. The thematic areas we wish to broaden include stem cell biology, tissue engineering, vertebrate models of human orthopedic disease, and the biochemistry and molecular biology of bone, cartilage and disc. We seek individuals with Ph.D., M.D., M.D./Ph.D., or equivalent degrees; postdoctoral experience; a record of publication in high-quality journals; and the ability to secure external funding. Ample opportunities exist for scientific interaction and collaboration within the department, throughout the university, and with other world-class institutions in the greater Philadelphia area. Successful candidates will be expected to establish innovative, externally-funded research programs. There is an excellent start-up package and protected time for research activities.

Applicants should submit their *curriculum vitae*, a research program summary, a statement of future plans, and the names and contact information of three references electronically to Susan Randolph, Administrator (**susan.randolph@Jefferson.edu**).

Thomas Jefferson University is an EEO/AA Educator, Employer.

Cleveland Clinic

VISION RESEARCH SCIENTISTS
Cole Eye Institute

In conjunction with a major expansion of the vision research program in the Cole Eye Institute, applications are being accepted for full-time research positions at the Assistant, Associate or Full Professor levels. Basic and clinician scientist with training in molecular genetics, molecular biology, cell biology, oncology, pharmacology, physiology, biophysics, biochemistry, developmental biology or gene therapy with research interests that are focused on understanding basic mechanisms related to the clinical areas of macular degeneration, inherited retinal diseases, glaucoma or cornea disorders will be seriously considered. Excellent laboratory space, generous start up funds, outstanding salary support and benefits package are included. Applicants for positions at Associate and Full Professor level must have a solid record of independent funding and ongoing grant support.

Interested applicants should submit a statement of their research interests related to one or more the above areas, a copy of their curriculum vitae, and contact information for three references to:

Joe G. Hollyfield, Ph.D.
Chairman, Ophthalmic Research
Cole Eye Institute (i31)
Cleveland Clinic
9500 Euclid Avenue
Cleveland, Ohio 44195-5245
Fax: (216) 445-3670
E-mail: hollyfj@ccf.org

CCF is an Equal Opportunity/Affirmative Action Employer.

VANDERBILT UNIVERSITY School of Medicine

The **Department of Biochemistry at Vanderbilt University School of Medicine** is seeking applicants for a tenure-track faculty position at the rank of Assistant, Associate, or Full Professor. The successful candidate will be expected to establish an innovative research program, educate graduate/medical students, train post-doctoral fellows, and participate in service activities within Vanderbilt and the scientific community. A generous start-up package and laboratory space will be provided. The Biochemistry Department currently has internationally recognized researchers in the areas of cell signaling, cell cycle checkpoints, cancer biology, neurobiochemistry, enzymology, mass spectrometry, and structural biology. Applicants will be evaluated primarily on the strength of their research program. All research areas and experimental approaches will be considered. However, we are especially interested in candidates with interests in epigenetics, DNA repair, DNA replication, cell cycle control or other research areas that complement the existing strengths within the Genome Maintenance Program of the Vanderbilt-Ingram Cancer Center.

Please forward an electronic cover letter, *curriculum vitae*, contact information for three references, and description of research program as a single pdf file to **marlene.jayne@vanderbilt.edu**.

Alternatively, mail hard copies of these materials to:
Biochemistry Faculty Search
Vanderbilt University School of Medicine
c/o Marlene Jayne
607 Light Hall
Nashville, TN 37232

The application deadline is **October 31, 2010** but applications will be evaluated as they arrive.

Women and minority candidates are especially encouraged to apply.

UBC

Canada Research Chair in Conservation Ecology Departments of Botany and Zoology

The Departments of Botany and Zoology at the University of British Columbia invite applications for a Tier 2 Canada Research Chair (CRC) in Conservation Ecology. This is a tenure track position, with initial appointment to be made at the Assistant Professor level, beginning no earlier than July 1, 2011. We seek outstanding applicants who address fundamental research questions in fields of Conservation Ecology complementary to existing strengths in UBC's Biodiversity Research Centre (**www.biodiversity.ubc.ca/index.html**). Our primary interest is in candidates whose research program includes terrestrial plant systems. Information about the CRC program can be found at **www.chairs.gc.ca**. Applicants must have a PhD, and preferably postdoctoral experience. The successful applicant will become a part of the Biodiversity Research Centre, whose members have recently been brought together in a new building containing research spaces and laboratories, as well as the Beaty Biodiversity Museum. A companion search is underway for a Plant Ecologist to be hired at an Associate Professor level.

Responsibilities of the position include establishing and conducting an internationally competitive, externally funded, research program, effective teaching at the undergraduate and graduate levels, supervising graduate students and performing service duties for the departments, university, and academic/scientific community.

Canada Research Chairs are open to individuals of any nationality; offers will be made in accordance with Canada Immigration requirements associated with the Canada Research Chairs Program. The position is subject to review and final approval by the CRC Secretariat.

View full posting and apply at **www.hr.ubc.ca/careers/faculty_postings.html**, Job ID 8560. Screening of applications will begin **November 15, 2010**.

Associate Professor in Plant Ecology Department of Botany

The Department of Botany at the University of British Columbia invites applications for a Plant Ecologist to be hired at an Associate Professor level. Applications are encouraged from advanced Assistant Professors who are competitive for tenure, as well as from those already appointed at an Associate Professor level. The appointment begins no earlier than July 1, 2011. We seek outstanding applicants who address fundamental research questions in any area of Plant Ecology. The successful applicant will become a part of the Biodiversity Research Centre (**www.biodiversity.ubc.ca/index.html**), whose members have recently been brought together in a new building containing research spaces and laboratories, as well as the Beaty Biodiversity Museum. A companion search is underway for a Conservation Ecologist to be hired at an Assistant Professor level.

Responsibilities of the position include conducting an internationally competitive, externally funded research program, teaching at undergraduate and graduate levels, supervising graduate students, and performing service duties for the department, university, and academic/scientific community.

View full posting and apply at **www.hr.ubc.ca/careers/faculty_postings.html**, Job ID 8561. Screening of applications will begin **November 15, 2010**.

UBC hires on the basis of merit and is committed to employment equity. All qualified persons are encouraged to apply. However, Canadians and permanent residents of Canada will be given priority.

Department of Molecular Physiology and Biophysics
Faculty Positions
Cell and Molecular Physiology of Skeletal Muscle

The Department of Molecular Physiology and Biophysics seeks outstanding candidates for tenure-track positions at any rank. Successful candidates are expected to establish independent laboratories focusing on the cellular and molecular mechanisms underlying the biology of skeletal muscle in health and disease. We are particularly interested in individuals who would complement existing strengths in the Iowa Center for Muscular Dystrophy Research.

These positions feature outstanding research space with state-of-the-art shared instrumentation, as well as substantial startup funds for equipment, personnel support and supplies. The University of Iowa is located in Iowa City, an affordable college community with many cultural amenities.

All applicants must have a relevant doctoral degree, productive research experience, and a strong record of research accomplishment. Candidates are judged on their potential to initiate and maintain a creative, independent research program, and their desire to train students and postdoctoral fellows.

To apply for a position, please visit the University of Iowa website at **http://jobs.uiowa.edu/faculty/view/58347**. Applicants should include a CV, letter of interest, and the names of three references. In addition, please send your CV directly to **Dr. Kevin P. Campbell, Head of the Department of Molecular Physiology and Biophysics, at kevin-campbell@uiowa.edu**. Consideration of completed applications will begin on **November 1, 2010**. Questions may also be directed to Dr. Campbell. Information about the Department and the Muscular Dystrophy Center can be found at **www.physiology.uiowa.edu**.

The University of Iowa is an Equal Opportunity/Affirmative Action Employer. Women and minorities are strongly encouraged to apply.

Tenure-Track Faculty Position in Chemistry or Chemical Biology Sloan-Kettering Institute

Sloan-Kettering Institute (www.ski.edu) is seeking an innovative individual at the Assistant Member level, with strong research accomplishments in synthetic or mechanistic organic chemistry, or chemical biology to establish a research program which addresses problems relating to bioorganic chemistry and cancer research. Faculty will be eligible to hold graduate school appointments in the Gerstner Sloan-Kettering Graduate School of Biomedical Sciences, the Weill Graduate School of Medical Sciences of Cornell University, as well as the Tri-Institutional MD/PhD Training Program and Tri-Institutional Training Program In Chemical Biology.

MSKCC offers a unique and exciting research environment with programs in Chemistry, Pharmacology, Immunology, Molecular Biology, Computational Biology, Genetics, Cell Biology, Developmental Biology, Cancer Pathogenesis and Structural Biology. The presence on campus of world-renowned clinical programs in cancer research, treatment and prevention offers many opportunities for creative collaboration.

Applicants must have a Ph.D. in chemistry, biochemistry, chemical biology, or pharmacology, and a dedication to engage in collaborative research efforts at the interface of chemistry and biology. Both a strong record of achievement and the potential to secure external funding are required.

The deadline for applications is November 1, 2010. Interested candidates should visit **http://facultysearch.ski.edu** to access the on-line faculty application. Please visit the site as soon as possible, as it contains important information on the required application materials, including deadlines for submission of letters of reference. Inquiries may be sent to **Marie Aiello at aiellom@mskcc.org** or to **Dr. David Gin, Search Committee Chair, Molecular Pharmacology & Chemistry Program at gind@mskcc.org**.

MSKCC is an equal opportunity and affirmative action employer committed to diversity and inclusion in all aspects of recruiting and employment. All qualified individuals are encouraged to apply.

Memorial Sloan-Kettering Cancer Center
www.mskcc.org

MOUNT SINAI SCHOOL OF MEDICINE

Tenure-track Faculty Positions in Immunology

The Mount Sinai Immunology Institute is seeking outstanding scientists to develop rigorous independent research programs in basic or translational immunology. Applicants whose programs address inflammatory bowel disease, gut-microbiome interactions, mucosal immunity, and intravital imaging are encouraged to apply. The Immunology Institute is a diverse, interactive group interested in basic and translational immunology and mechanisms of immune-mediated diseases, **http://research.mssm.edu/iisinai**. Applicants may have an MD, PhD or MD/PhD degrees and may be appointed at the Assistant, Associate or Full Professor levels, at Mount Sinai School of Medicine with a generous start-up package.

Applicants should submit a CV, research plan and the names of three references to: **Immunology Institute Faculty Search Committee, email: Zaida.Newman@mssm.edu**. Review of applications will begin **September 2010.**

Duke University Medical Center

The Department of Biochemistry, Duke University Medical Center (www.biochem.duke.edu), invites applications for multiple faculty positions at the Assistant and Associate Professor levels. We welcome candidates in all areas of biochemistry and biomolecular sciences. The successful candidate will be expected to establish a strong, independent research program and to participate in departmental teaching and service.

Electronic applications in PDF format (preferably as a single file) should include a curriculum vitae and summary of research interests, and should be sent to: **facultysearch-biochem@win.duke.edu**.

Recommendation letters (PDF) should be sent by **three referees** to: **rec-biochem@win.duke.edu**. Consideration of applications will commence in November 2010.

Duke University is an Equal Opportunity/Affirmative Action Employer.

UCI
University of California, Irvine

FACULTY POSITION IN PHARMACOLOGY

The Department of Pharmacology at the University of California, Irvine (UCI) invites applications for a tenured faculty position at the level of Associate/Full Professor. We seek a scholar with a proven record of research accomplishments. He/she should have specific interest in cellular and molecular mechanisms governing gene expression and their functional links to physiology and metabolism. Special consideration will be given to candidates with expertise and experience in integrating genetic, biochemical and physiological approaches. Other qualifications include an M.D. and/or Ph.D. and a strong drive to pursue a dynamic research program and an interest in and talent for graduate teaching.

Interested applicants must submit cover letter, curriculum vitae, a statement of research, a statement of teaching and contact information for 3-5 references via the University of California Irvine's Academic Personnel RECRUIT System at **http://recruit.ap.uci.edu**.

The University of California, Irvine has an active career partner program and an NSF ADVANCE Program for Gender Equity and is an Equal Opportunity Employer committed to excellence through diversity.

Bioenergy Assistant Professor Positions
Colorado State University

Colorado State University

Colorado State University is recruiting candidates for three tenure-track assistant professor positions in bioenergy. These new faculty members will interact closely with several successful bioenergy programs in education, research, and technology transfer at CSU, including an NSF IGERT Ph.D. program, the Sustainable Bioenergy Research Center, the Clean Energy Supercluster, and the industry-sponsored Colorado Center for Biofuels and Biorefining.

- **Department of Chemical and Biological Engineering**
  - Applicants with interests and expertise in synthetic biology, including protein and metabolic engineering, are particularly encouraged.
  - Ph.D. or equivalent in chemical or biological engineering, or related field, is required by January 2011.
  - **https://www.engr.colostate.edu/cheme/search/**
  - Applications will be reviewed starting **September 30, 2010**.
- **College of Agricultural Sciences**
  - Applicants with expertise in agricultural aspects of biofuel development are sought. The area of emphasis could be (but is not limited to) feedstock production systems, byproduct utilization, or life cycle analysis.
  - Postdoctoral research experience is encouraged but not required.
  - **http://www.agsci.colostate.edu/biofuels_position.html**
- **Department of Biology**
  - Applicants will work on molecular and biochemical aspects of algal cell biology that are relevant to biofuel development. Example areas of emphasis include energy transduction pathways, carbon metabolism, or growth.
  - Postdoctoral research experience is encouraged but not required.
  - **http://www.biology.colostate.edu/employment**

Applications from candidates with the ability to advance the University's commitment to diversity and multiculturalism through research, teaching, and outreach with relevant programs, goals, and activities are particularly encouraged. CSU is an EO/AA Employer. Colorado State University conducts background checks on all final candidates.

The University of Texas at Austin Cell Biology Position

The Section of Molecular Cell and Developmental Biology invites applications for a tenure-track Assistant Professor position. We seek an outstanding investigator who will build an active research program in eukaryotic cell biology and who will teach effectively at the undergraduate and graduate levels. The successful applicant will be joining the biology community at UT-Austin during an exciting phase of growth, with recent hires in cell biology, developmental biology, plant biology, neuroscience, systems biology, and related areas. Very generous start-up funds are available, and the successful candidate will also be eligible for affiliation with the Institute for Cellular and Molecular Biology, which provides state-of-the-art facilities and supports an excellent graduate program.

Austin is located in the Texas hill country and is widely recognized as one of America's most beautiful and livable cities.

Please send a single PDF file containing your curriculum vitae, summary of research interests and names of three references to: **MCDB_cell_bio@biosci.utexas.edu**. References may also send their letters directly to the same email address. Applications received by **November 1, 2010** will receive first consideration, but applications will continue to be accepted until the position is filled.

Home pages: **http://www.biosci.utexas.edu/MCDB/** and **http://www.icmb.utexas.edu/**

The University of Texas, Austin is an Equal Opportunity Employer that values diversity in its work force. Women and minorities are encouraged to apply; a background check will be conducted on applicant selected.

Western University of Health Sciences
The discipline of learning. The art of caring.

DEAN, GRADUATE COLLEGE OF BIOMEDICAL SCIENCES

Western University of Health Sciences (WesternU) is a rapidly growing, thriving center for graduate health care and veterinary education. WesternU's core values have propelled the University to impeccable levels of excellence.

In 2009, WesternU added four colleges – Dental Medicine, Optometry, Podiatric Medicine and Graduate Biomedical Sciences to its existing colleges of Osteopathic Medicine, Allied Health, Graduate Nursing, Pharmacy and Veterinary Medicine.

This year, WesternU completed the construction of a 178,000 square foot Health Education Center that added 26,556 square footage of new research space, and a 78,000 square foot Patient Care Center.

WesternU provides a truly innovative and medically relevant research infrastructure that brings together researchers with synergistic expertise and projects in three thematic areas that are represented by three developing centers of excellence: Center for Molecular and Metabolic Diseases, Center for Infectious Diseases and Immunology, and Center for Integrative Neurobiology.

WesternU recently embarked on a long-range program to enhance its standing as a graduate academic health science center committed to expanding its institutional research presence. The establishment of the Graduate College of Biomedical Sciences (GCBS) reflects this commitment and places WesternU in a prominent role for health-related research and training.

The GCBS was created to train highly skilled and caring biomedical researchers and future practitioners for entry into academia, industry or the medical professions. To that end, the GCBS strives to graduate humanistic professionals who will produce new biomedical knowledge and practice their healthcare professions with a deeper and broader understanding of the dynamic sciences underlying the treatment of their patients. The GCBS offers three individual programs: Master of Science in Biomedical Sciences, Master of Science in Pharmaceutical Sciences, and as of summer 2010, Master of Science in Medical Sciences. The University Strategic Plan calls for an expansion of these programs, other appropriate master degree level offerings in the biomedical sciences, and the development of innovative PhD programs in selected disciplines.

WesternU seeks an active researcher with administrative academic acumen to provide visionary leadership and strategic direction to the GCBS. The Dean will oversee the day to-day operations of all graduate programs leading to an advanced degree in the biomedical sciences within the GCBS. The selected candidate will be an individual who possesses superior leadership, management, operational, communication and external networking skills.

Position qualifications include a PhD or equivalent with a minimum of ten (10) years experience at a medical or graduate school and/or a research institute. Academic administrative experience and a successful history of recent NSF/NIH funding are required. Candidates must meet the criteria for faculty appointment at the level of professor, tenured. Additional details on the position can be found at our website: **https://jobs.westernu.edu/applicants/jsp/shared/Welcome_css.jsp**. Please direct application materials to:

Dr. Philip Nelson, Chair
Dean CGBS Search Committee
Western University of Health Sciences
309 East Second Street
Pomona, CA 91766-1854
Email: pnelson@westernu.edu

Please apply by **October 31, 2010**. The position will remain open until filled.

Western University of Health Sciences is an Equal Opportunity Employer.

Director
Division of Medical Genetics

Department of Human Genetics
Emory University, Atlanta, Georgia

EMORY UNIVERSITY SCHOOL OF MEDICINE

The Department of Human Genetics at Emory University School of Medicine is seeking a Director for the Division of Medical Genetics. We seek an outstanding clinician scientist to lead a comprehensive and vibrant medical genetics program with outpatient services, including general, specialty and outreach genetics clinics, and inpatient consultations at Children's Healthcare of Atlanta. The position will also include a leadership role in the Medical Genetics residency program and participation in training of graduate students, medical students and residents.

The Department of Human Genetics, founded in 2001, is both a basic science and clinical department with 53 faculty members, including 14 who are ABMG certified. The Department, recently ranked 6th in NIH funding for genetics departments, has an exceptional research program with many faculty involved in translational and/or clinical research (see **www.genetics.emory.edu**). In addition, the Department hosts Emory Genetics Laboratory, a clinical laboratory that specializes in rare disease testing and continues to be a leader in technology advancements. The unique combination of fully-fledged basic research faculty, along with the comprehensive clinical genetics program, places the Department at the forefront of contemporary translational research and predictive health.

Emory University consistently ranks among the top 20 research universities and is the largest healthcare system in Georgia, serving more than 5 million individuals. It also boasts strong academic training programs and recently earned high ranking among academic institutions in the "Best Places to Work for Postdocs".

The qualified candidate must hold an M.D. or M.D./Ph.D. degree and be ABMG board-certified in Clinical Genetics. Experience in leadership positions and an outstanding track record in research are also required. Although substantial resources will be made available to qualified candidates, exceptional candidates have the potential for an appointment as an endowed professor.

Please send CV, cover letter, and names of 3 potential references to:

Dr. Christa Lese Martin, Ph.D.
Department of Human Genetics, Emory University School of Medicine
615 Michael St., Suite 301, Atlanta, GA 30322
or clmartin@genetics.emory.edu

Basic/Translational Researcher

The University of Pittsburgh Department of Neurological Surgery is recruiting an experienced basic/translational researcher for a Research Assistant Professor position. Candidates should have a doctoral degree and at least five years of post-doctoral experience. Candidates will be responsible for the overall coordination of all research efforts in our Neuroapoptosis Laboratory including the writing and editorial assistance of progress reports, manuscripts, grant proposals and IACUC protocols. Salary is competitive and commensurate with training and experience.

Send inquiries to:

Robert M. Friedlander, M.D.
Chairman
Department of Neurological Surgery
Suite B-400 PUH, 200 Lothrop Street
Pittsburgh, PA 15213
(412) 647-6358
Friedlanderr@upmc.edu

The University of Pittsburgh is an Affirmative Action, Equal Opportunity Employer.

RUTGERS

Two Assistant Professors of Cell Biology and Neuroscience

The Department of Cell Biology and Neuroscience at Rutgers, The State University of New Jersey, Piscataway, seeks to fill two tenure-track positions at the Assistant Professor level. The first of these positions will be filled by an individual working on adult onset neurodegenerative disease including, but not limited to Alzheimer's disease, ALS and SMA. This individual will also have an appointment in the emerging Rutgers Brain Health Institute, which maintains strong ties to the biotech and pharmaceutical industries in the area. The second position will be filled by an individual with experience and interest in the use of human stem cells, in particular iPSCs, and their application to the biology of pluripotency or developmental neurobiology. This individual will have laboratory space in the Rutgers Stem Cell Research Center and will have access to large numbers of cell lines derived from well-defined neurological conditions and genetic disorders through The Rutgers Cell & DNA Repository. The Department is part of the Division of Life Sciences, a group of Departments and Institutes with research foci ranging from biomaterials and nanotechnology to human genetics.

Applicants should have a Ph.D. and/or M.D. with a minimum of three years postdoctoral experience. The successful candidate will be expected to establish an independent research program supported by external funding and to contribute to undergraduate and graduate education. The Department offers excellent facilities and competitive start-up packages. Interested individuals are encouraged to apply online through the CBN website (**http://cbn.rutgers.edu**). Review of applications will begin immediately on a rolling basis.

Rutgers University is an Equal Opportunity/Affirmative Action Employer.

University of Minnesota Tenure-Track Assistant Professor in Systems and Computational Biology

The Department of Biochemistry, Molecular Biology and Biophysics invites applications for a full-time, tenure-track Assistant Professor position to begin on or around July 1, 2011. We seek candidates whose expertise complement existing Departmental strengths and who integrate systems level approaches and computational tools for the study of metabolic disease and/or cancer. For more details about the Department please consult: **http://cbs.umn.edu/BMBB/**.

The successful candidate will be expected to develop a strong, externally funded research program and contribute to the interdisciplinary undergraduate, graduate and professional teaching programs of the University. Preference will be given to candidates seeking to use cutting-edge genomic, proteomic and/or metabolomic technologies along with computational tools to gain biological insights at a systems level. Establishing collaborative partnerships across disciplines will be strongly encouraged. All candidates must have a Ph.D. and/or MD degree, applicable postdoctoral experience and a strong publication record.

The successful candidate will receive a substantial start-up package to establish their laboratory and a salary commensurate with education and experience. We will begin reviewing applications immediately and continue until the position is filled. Please apply online at **employment.umn.edu**, click on **"Search Postings"** and enter **168329** into the requisition number field. Please attach curriculum vitae and a brief statement of research plans (not to exceed 5 pages). Three letters of recommendation that consider both research and teaching potential should be sent to the **Faculty Search Committee, c/o Ms. Ann Johnson, Department of Biochemistry, Molecular Biology and Biophysics, University of Minnesota, 6-155 Jackson Hall, 321 Church Street S.E., Minneapolis, MN 55455** or as an attachment to **swans143@umn.edu**.

The University of Minnesota is an Equal Opportunity Educator and Employer. The Department of Biochemistry, Molecular Biology and Biophysics strongly encourages all individuals to apply regardless of gender, ethnicity or background and is committed to a diverse research and teaching environment.

Assistant Professor of Microbiology

The Department of Microbiology invites applications from Ph.D.-level scientists for **a tenure-track position at the level of ASSISTANT PROFESSOR**. The Department's 15 faculty members and affiliated units at the University have broad research strengths in microbiology, immunology, immunity and host defense, microbial pathogenesis, virology, microbial physiology, genetics, genomics, environmental microbiology, and biotechnology. We are seeking outstanding candidates taking innovative, molecular and cellular approaches to the study of **Medical Microbiology**. This area is broadly defined and would include the study of viral, prokaryotic and or eukaryotic and prionic pathogens. The successful candidate will have had at least three years postdoctoral experience and will have published several articles in high impact peer-reviewed journals. He/She will be expected to establish a strong independent, extramurally funded research program and participate in the teaching of undergraduate and graduate courses. Research facilities that include new animal care and BSL III facilities, and competitive salary and start-up funds will be provided. Opportunities exist to establish strong collaborations with faculty in the Five College Area and at Bay State Medical Center.

Applicants should send a curriculum vitae, a statement of research and teaching interests, reprints of recent publications, and at least three letters of recommendation to: **Chair of Microbiology Search Committee, Department of Microbiology, University of Massachusetts, N203 Morrill IV North, Amherst, MA 01003; microbio-dept@microbio.umass.edu.** The search committee will begin reviewing applications on **October 18, 2010** and will continue until the position is filled. Hiring is contingent upon the availability of funds.

The Five College Consortium, comprised of Smith College, Amherst College, Mount Holyoke College, Hampshire College, and the University of Massachusetts Amherst, provides an intellectual environment committed to providing academic excellence and diversity including mentoring programs for faculty. The College and the Department are committed to increasing the diversity of the faculty, student body and the curriculum. The University of Massachusetts is an Affirmative Action/Equal Opportunity Employer. Women and members of minority groups are encouraged to apply.

University of Minnesota
Medical School

Department of Pharmacology (with potential joint appointment in the Institute for Translational Neuroscience) TENURE/TENURE TRACK POSITION (Assistant Professor, Associate Professor, Professor)

The Department of Pharmacology at the University of Minnesota invites applications for a tenure/tenure track faculty position (Assistant, Associate or Full Professor). Applicants using molecular, biochemical, cellular, and/or integrative translational approaches to study problems relevant to pharmacological sciences are encouraged to apply. Positions are also available in this joint recruitment with the Institute for Translational Neuroscience, whose interest is in how basic science discoveries may lead to new therapeutic principles of certain neurological disorders (see their website for more details). Qualifications include a Ph.D. in biomedical science, or an M.D. degree, and relevant postdoctoral research experience. Applicants must have a strong record of research accomplishments, as documented by publications in leading peer-reviewed journals. The successful **Assistant Professor** candidate will be expected to develop an innovative, competitive research program supported by extramural funding and to participate in departmental teaching activities. Applicants for **Associate Professor and Professor** positions must demonstrate distinction in published research, evidence of consistent extramural funding, and a commitment to teaching. For additional information about the department and the Institute for Translational Neuroscience, visit: **www.pharmacology.med.umn.edu** and **http://www.itn.umn.edu**.

Interested applicants should apply online at **http://employment.umn.edu/applicants/Central?quickFind=88959** for the **Assistant Professor** position or at **http://employment.umn.edu/applicants/Central?quickFind=88961** for the **Associate Professor or Professor** position, and attach a letter of interest, curriculum vitae, brief statement of research interests, and contact information for three references.

University of Pittsburgh

The newly established **Department of Developmental Biology** at the University of Pittsburgh School of Medicine is seeking a highly qualified individual to fill a tenure track position at the **Assistant/Associate Professor level**. Outstanding candidates with research expertise in the field of systems biology/computational biology are encouraged to apply. The successful candidate is expected to establish a high quality independent research program in systems biology and will have the opportunity to collaborate with faculty members of Development Biology in projects related to gene regulatory networks, whole genome analysis, and statistical genetics as they are related to development. Currently the department has research interests in human stem cell biology, regenerative medicine, and in cardiovascular, renal and liver development. The department also has ongoing research focused on elucidating developmental mechanisms that impinge on human diseases. In accordance with the multidisciplinary research activities of the appointee, the appointee may be offered a secondary appointment in the Dept. of Computational and Systems Biology of the University of Pittsburgh School of Medicine. In addition, the appointee may have unique opportunities to collaborate with faculty and researchers at the Pittsburgh Supercomputing Center and Carnegie Mellon University. For more information about the Dept. of Developmental Biology, please go to: **www.devbio.pitt.edu**.

Applicants should have a Ph.D. degree and are invited to send their CV, a short summary of research interests and future research plans, and names of three referees by **November 30th, 2010** to: **dbsearch@pitt.edu**; **Faculty Search Committee, Department of Developmental Biology, 530 45th Street, 8111 Rangos Research Center, Pittsburgh, PA 15201, USA**.

The University of Pittsburgh is an Equal Opportunity, Affirmative Action Employer.

Wayne State University

Tenure/Tenure Track Faculty Positions in Biological Sciences

The Department of Biological Sciences at Wayne State University has multiple tenure track openings for new faculty. Rank will be dependent upon qualifications. Preference will be given to candidates who use innovative approaches to study complex biological problems using animal, plant or microbial models.

Physiology: Areas of interest include, but are not limited to, neurobiology, cellular and intercellular signaling and the role of regulation in the aging process.

Developmental Biology: Areas of interest include, but are not limited to, epigenetics, comparative development processes, developmental plasticity and regeneration. Animal and plant systems are equally welcome.

Microbiology: Areas of interest include, but are not limited to, bacteriology, virology, immunology, host-pathogen interactions, and infectious disease processes.

Wayne State University is a large, comprehensive, nationally ranked research institution that offers state-of-the-art research facilities and highly competitive start-up packages. The metropolitan Detroit area offers a rich cultural and educational environment, an excellent standard of living, and easy proximity to Michigan's lakes, forests and recreational sites.

Applicants must have a Ph.D. degree, postdoctoral experience and an outstanding record of research achievement. Successful applicants are expected to establish and maintain vigorous, externally funded research programs and to participate in graduate and undergraduate education. All positions are posted online at jobs.wayne.edu. In addition to an online application that includes cover letter and curriculum vitae, applicants must submit a 2-page statement of their research plans and have three letters of reference sent to: **Faculty Search Committee, Department of Biological Sciences, Wayne State University, 5047 Gullen Mall, Detroit, MI 48202**. Please apply by **November 1, 2010** for full consideration. Applications will be considered only when all materials have been received.

Wayne State University is an Affirmative Action/Equal Opportunity Employer. Women and members of minority groups are especially encouraged to apply.

NORTHWESTERN UNIVERSITY

ASSISTANT PROFESSOR

The **Department of Molecular Biosciences** encourages outstanding individuals with research interests that complement existing strengths of the department to apply for a tenure-track appointment at the level of Assistant Professor. The department is an exciting interdisciplinary research and training environment located on Northwestern's Evanston, Illinois campus (**http://www.molbiosci.northwestern.edu**). Current faculty research interests encompass biochemistry, cell and developmental biology, structural biology and molecular biology.

We are particularly interested in the area of Cellular and Molecular Biology, especially applicants whose research utilizes creative imaging approaches to investigate dynamic cellular processes.

Applicants should prepare a cover letter, curriculum vitae, statement of teaching experience and interests, research summary, and a statement of future research goals. For further instructions and to submit the application, please visit the Molecular Biosciences homepage at **http://www.molbiosci.northwestern.edu**. Applicants should arrange for at least three letters of recommendation to be submitted on their behalf. Questions should be sent to **molbioscisearch@northwestern.edu**.

To ensure full consideration, please submit all materials by **November 1, 2010**.

Northwestern University is an Affirmative Action/Equal Opportunity Employer. Women and underrepresented minorities are especially encouraged to apply.

CASE WESTERN RESERVE UNIVERSITY
SCHOOL OF MEDICINE

Faculty Positions
Department of Pharmacology

Applications are invited for faculty positions in the growing and newly renovated Department of Pharmacology at the Case Western Reserve University School of Medicine. All faculty ranks are open, dependent on current level of achievement. The Department has a long tradition of excellence in molecular pharmacology with strong growing programs in chemical biology, membrane structural biology, pharmacogenetics/genomics, and translational pharmacology. Candidates in any area relevant to modern pharmacology will be competitive, but those with previous education or research experience in pharmacology are especially invited to apply.

Visit **http://pharmacology.case.edu/** for more information about the department.

Interested scientists should submit a cover letter, full curriculum vitae including publications and grant support, and a list of professional references. In addition, applications should include descriptions of the candidate's research interests and goals, and teaching, mentoring, and professional service experiences. Qualified applicants for instructor should hold a doctoral degree along with significant postdoctoral experience. Applicants for Assistant Professor should provide a record of scholarly achievement and the potential to advance independently in a field of research. For senior ranks, requirements include evidence of excellent research and recognition of the research program at a national/international level. Rank is commensurate with experience and achievement.

Please submit applications by e-mail to **Camala Thompson, Programs Administrator (cami@case.edu)**, with **c.c. to Amy Wilson-Delfosse, Ph.D., Associate Professor of Pharmacology (axw41@case.edu)**.

In employment, as in education, Case Western Reserve University is committed to Equal Opportunity and Diversity.

UT SOUTHWESTERN MEDICAL CENTER

Assistant Professor
Biochemistry

The Department of Biochemistry at The University of Texas Southwestern Medical Center invites applications from candidates for a tenure-track faculty position at the rank of Assistant Professor. Candidates should be engaged in innovative research within the broad fields of biochemistry or molecular biology. UT Southwestern maintains state-of-the-art facilities and employs a faculty that includes four Nobel Laureates and eighteen members of the National Academy of Sciences. The Biochemistry Department offers a vibrant environment for research, generous start-up support, and participation in graduate-level teaching.

Applicants should submit a *curriculum vitae*, a concise description of research plans and three letters of reference by **October 31, 2010** to **Steven L. McKnight, Chair, Department of Biochemistry (biochem.search@utsouthwestern.edu)**.

The University of Texas Southwestern Medical Center is an Affirmative Action/Equal Opportunity Employer. Women and minority candidates are encouraged to apply.

UT SOUTHWESTERN MEDICAL CENTER

Assistant Professor
Biochemistry

The Department of Biochemistry at The University of Texas Southwestern Medical Center invites applications from qualified candidates for a tenure-track faculty position at the rank of Assistant Professor. We are seeking a mass spectrometrist engaged in innovative research in the field of proteomics. UT Southwestern maintains state-of-the-art facilities and employs a faculty that includes four Nobel Laureates and eighteen members of the National Academy of Sciences. The Biochemistry Department offers a vibrant environment for research, generous start-up support, and participation in graduate-level teaching.

Applicants should submit a *curriculum vitae*, a concise description of research plans and three letters of reference by **October 31, 2010** to **Steven L. McKnight, Chair, Department of Biochemistry (proteomics@utsouthwestern.edu)**.

The University of Texas Southwestern Medical Center is an Affirmative Action/Equal Opportunity Employer. Women and minority candidates are encouraged to apply.

Assistant or Associate Professor of Pharmaceutics and Drug Delivery

The Department of Pharmaceutical Sciences invites applications for a tenure-track or tenured faculty position.

The candidate should have demonstrated research productivity through a focused research program in Pharmaceutics and Drug Delivery. The successful candidate will be expected to establish an extramurally-funded research program, participate in both professional PharmD and graduate teaching, and service. Applicants with current transferable funding will be given a priority. The Department of Pharmaceutical Sciences houses the Center for Drug Discovery, New England Inflammation and Tissue Protection Institute, the Center for Pharmaceutical Biotechnology and Nanomedicine, and the Center for Translational Imaging. For additional information about the Department, please visit the website: http://www.pharmsci.neu.edu.

For more information about the position please contact Robert Schatz, Ph.D., Associate Professor of Toxicology and Search Committee Chair, at r.schatz@neu.edu.

How to Apply: Applications must be submitted on-line by visiting the College website at http://www.northeastern.edu/bouve/ and click on "Faculty Positions". Applicants should submit a formal letter of interest, along with curriculum vitae, and names and addresses of three references.

Northeastern University in an Equal Opportunity/Affirmative Action, Title IX, and an ADVANCE institution.

Northeastern University
Bouvé College *of* Health Sciences
School *of* Pharmacy

http://www.neu.edu

STANFORD UNIVERSITY

Department of Biology
Faculty Position in Neural Circuits and Behavior

The Department of Biology at Stanford University welcomes applications for a tenure track faculty position at the Assistant Professor rank. We seek applicants interested in neural circuits and behavior. Examples of interest areas include, but are not limited to, the genetic dissection of neural circuits underlying perception and behavior using state-of-the-art techniques in electrophysiology, imaging and/or manipulation of intact neural circuits in a behavioral context. Applicants are expected to develop a vigorous research program and to participate in both undergraduate, graduate, and postdoctoral education and training. For information about the Department consult **http://biology.stanford.edu/**.

Applicants are requested to provide a cover letter, a curriculum vitae including publication list, a statement of research accomplishments and future research plans, a description of teaching experience, and three letters of recommendation.

Interested candidates should apply online at **AcademicJobsOnline.Org (https://academicjobsonline.org/ajo/jobs/340)**.

Applicant materials must be received by **November 15, 2010**. The appointment would begin September 1, 2011.

Stanford University is an Equal Opportunity Employer and is committed to increasing the diversity of its faculty. It welcomes nominations of and applications from women and members of minority groups, as well as others who would bring additional dimensions to the university's research, teaching, and clinical mission.

The Jackson Laboratory
leading the search for tomorrow's cures

Faculty Recruiting

The Jackson Laboratory, a mammalian genetics research institution in Bar Harbor, Maine, is hiring Assistant, Associate and Full Professors. Faculty members are being recruited for research in diverse areas, including:

- Cancer Biology
- Computational Biology and Bioinformatics
- Comparative Mouse and Human Genomics
- Genetics of Complex Traits
- Neuroscience
- Stem Cell Biology
- Developmental Biology
- Immunology/Inflammation
- Metabolic Disease/ Aging Research

Candidates should have a Ph.D., M.D., or D.V.M. with an exceptional record of research accomplishment. The ability to develop a competitive, independently funded research program is essential.

The Jackson Laboratory offers a uniquely collaborative scientific research environment. Faculty is supported by outstanding scientific support services, unparalleled mouse and genomic resources, postdoctoral and predoctoral training programs, and numerous courses and conferences centered on the mouse as a genetic model for human biology and disease.

Applicants should submit a curriculum vitae and a statement of research interests and plans online to: www.jax.org/careers, click on Faculty Positions. In addition, please arrange to have three letters of reference sent to: facultyjobs@jax.org

The Jackson Laboratory is an EOE/AA employer.

The Jackson Laboratory, 600 Main Street, Bar Harbor, Maine 04609

Faculty Positions: Center for Cell Engineering

The Center for Cell Engineering (CCE) at Memorial Sloan-Kettering Cancer Center is seeking innovative individuals, for tenure-track positions at the Assistant Member level, with strong research accomplishments in stem cell research, cell engineering and/or cell therapy. Applicants may be considered for appointment in the Molecular Pharmacology and Chemistry, Immunology or Developmental Biology Programs of the Sloan-Kettering Institute (http://www.ski.edu). Qualified applicants with an MD degree may be offered a joint appointment in an appropriate department in Memorial Hospital. Faculty will be eligible to hold appointments in the Gerstner Sloan-Kettering Graduate School of Biomedical Sciences, the Weill Cornell Graduate School of Medical Sciences, as well as the Tri-Institutional MD/PhD Training Program.

The CCE focuses on research leading to innovative cell therapies and the clinical translation thereof. Successful applicants will have access to outstanding resources, including state-of-the-art facilities for cGMP cell processing, cell purification, imaging, vector production, transgene monitoring, genomic analyses and chemical screens. MSKCC offers a unique and exciting research environment with programs in, Pharmacology, Chemistry, Developmental Biology, Immunology, Molecular Biology, Computational Biology, Genetics, Cell Biology, Cancer Pathogenesis and Structural Biology. The presence on campus of world-renowned clinical programs in cancer research, treatment and prevention offers many opportunities for effective translational research.

Applicants should have an MD and/or PhD degree, productive postdoctoral experience, and dedication to important problems related to human cell engineering, including induced pluripotent stem cells, and the development of novel cell therapies.

The deadline for applications is **November 1, 2010**. Interested candidates should visit **http://facultysearch.ski.edu** to access the on-line faculty application. Please visit the site as soon as possible, as it contains important information on the required application materials, including deadlines for submission of letters of reference. Inquiries may be sent to Tiffany Lennon, at lennont@mskcc.org or to Dr. Michel Sadelain, Director, Center for Cell Engineering at **m-sadelain@ski.mskcc.org**. MSKCC is an equal opportunity and affirmative action employer committed to diversity and inclusion in all aspects of recruiting and employment. All qualified individuals are encouraged to apply.

Memorial Sloan-Kettering Cancer Center
www.mskcc.org

NORTHWESTERN UNIVERSITY

Neurobiology and Physiology
Tenure-Track Faculty Position

The Department of Neurobiology and Physiology, in the Weinberg College of Arts and Sciences, seeks to recruit a new faculty member at the Assistant Professor level. Applicants holding a Ph.D. and/or M.D. degree and demonstrating an outstanding record of scientific achievement will be considered. We are interested in individuals whose research addresses fundamental issues in neuroscience, including but not limited to molecular neuroscience, and who show significant potential for innovation, scholarship, and commitment to excellence in research and teaching.

Successful candidates will be expected to establish and maintain a high-profile research program attracting substantial extramural funding. The appointee will have access to state-of-the-art life science research support facilities and opportunities to interact with colleagues in the Institute for Complex Systems, Cognitive Neurobiology and Alzheimer's Disease Center, Center for Reproductive Science, Center for Sleep and Circadian Biology, Robert H. Lurie Comprehensive Cancer Center and an interdepartmental neuroscience graduate program with over 150 faculty.

Applicants will submit (in PDF format) a cover letter, a CV, and a description of research plans. For details on preparing the application, please visit **www.neurobiology.northwestern.edu**. Please plan to request at least three letters of recommendation. Applications received by **November 22, 2010** will be ensured full consideration. Please direct any questions to **nbpfacultysearch@northwestern.edu**.

AA/EOE. Women and minority applicants are encouraged to apply.

Faculty Position

Norris Cotton Cancer Center (NCCC), bridging Dartmouth Medical School (DMS) and Dartmouth-Hitchcock Medical Center (DHMC), seeks candidates for a tenured or tenure-track faculty position in the Molecular Biology of Cancer. Physicians at NCCC see over 400 new lung cancer patients annually, and our goal is to recruit an established investigator to participate in an interdisciplinary program of physicians and scientists focused on the etiology and treatment of lung cancer. Candidates should have an M.D., Ph.D., or both degrees; an outstanding academic record, and an externally funded research program relevant to cancer in scientific areas that might include (but not be limited to) cellular signaling, stem cell biology, genome stability, genomics, proteomics, drug discovery, and/or structural biology using modern experimental model systems. The successful candidate will be appointed in a scientifically appropriate academic DMS department at the rank of Associate or Full Professor and will be expected to participate in teaching/mentoring in the graduate and/or medical school.

NCCC is one of only 40 National Cancer Institute-designated comprehensive cancer centers in the United States with facilities at DHMC, rated by US News and World Report as one of the top 50 hospitals nationally. Laboratories at NCCC and DMS, which rank as one of the top 35 NCI grant recipients, are state-of-the-art, buttressed by a full spectrum of research support services, including genomic, proteomic, bioinformatics, imaging, transgenic animal and pathology core facilities. Additional information is available on the NCCC website: **http://www.cancer.dartmouth.edu/**.

Curriculum vitae, including extramural grant support, statements of research interests, administrative experience, and contact information for at least five references should be sent in PDF format to: **Lung.Faculty.Search@Dartmouth.edu**.

Review of applications will begin immediately and will continue until the position is filled.

Dartmouth is an Affirmative Action/Equal Opportunity Employer. Women and members of minority groups are strongly encouraged to apply.

THE LINDA AND JACK GILL CENTER FOR BIOMOLECULAR SCIENCE AT INDIANA UNIVERSITY, BLOOMINGTON, IN

ENDOWED PROFESSORSHIP IN CELLULAR/MOLECULAR NEUROSCIENCE

Indiana University – Bloomington and The Linda and Jack Gill Center for Biomolecular Science seek an outstanding senior-level molecular or cellular neuroscientist to join the Gill Center (**www.indiana.edu/~gillctr/**) as one of five endowed chairs. This position offers an attractive salary and start-up package, a generous annual endowment, and access to substantial core facilities. The Gill Center Laboratories are housed in a new (fall, 2009) research building. We specifically seek an individual with a record of outstanding research contributions, proven ability to secure sustained extramural funding, expertise in state-of-the- art molecular and cellular neuroscience techniques, and demonstrated leadership in their chosen field. A PhD and/or MD in a relevant discipline is required. The Gill Center was established by a generous gift from Linda and Jack Gill with a mission to address important neuroscience questions using cutting edge technology. Questions about the position can be directed to the interim director of the Gill Center, Ken Mackie (**kmackie@indiana.edu**).

Applicants should electronically submit dossiers, including a curriculum vitae, a statement of research accomplishments and future plans, representative publications, and the names of six references to **Misty Theodore** (**gillctr@indiana.edu**).Applications will be reviewed until the position is filled.

Indiana University is an Affirmative Action Employer. Applications from women and minority candidates are especially encouraged.

Gill Center

INDIANA UNIVERSITY BLOOMINGTON

HUNTSMAN CANCER INSTITUTE UNIVERSITY OF UTAH

UNIVERSITY OF UTAH HEALTH SCIENCES

The **Department of Oncological Sciences** at the **University of Utah** and **Huntsman Cancer Institute** invite applications for a tenure-track faculty position at the **assistant** or **associate professor** level. We seek a basic cancer biologist with an interest in early translational research, a PhD or MD/PhD, and a track record of scientific excellence. Research interests could include basic cellular mechanisms altered in cancer, tumor models, cancer genetics, and investigational therapeutics. Departmental strengths include epigenetics and transcriptional regulation, mouse and zebrafish models of cancer, and cancer cell biology, including signaling, apoptosis, motility, and metabolism. Huntsman Cancer Institute is an NCI-Designated Cancer Center with state-of-the-art laboratories and shared resources, including core facilities for imaging, genomics, drug screening, and population studies. We offer a collegial and interactive research environment that fosters the development of junior faculty and robust graduate programs for training PhD and MD/PhD students.

Candidates are encouraged to apply by **November 10, 2010**, with their curriculum vitae, a description of research interests and accomplishments and three letters of recommendation to:

Huntsman Cancer Institute, University of Utah
Attn: Recruitment Office, Room 5363
2000 Circle of Hope, Salt Lake City, UT 84112-5550
e-mail: hci.recruitment@hci.utah.edu

The University of Utah is an Affirmative Action/Equal Opportunity employer and does not discriminate based upon race, national origin, color, religion, sex, age, sexual orientation, gender identity/expression, disability, or status as a Protected Veteran. Upon request, reasonable accommodations in the application process will be provided to individuals with disabilities. To inquire about the University's nondiscrimination policy or to request disability accommodation, please contact: Director, Office of Equal Opportunity and Affirmative Action, 201 S. Presidents Circle, Rm 135, Salt Lake City, UT 84112 801-581-8365.

ASSISTANT PROFESSOR DEPARTMENT OF GENETICS HARVARD MEDICAL SCHOOL

The Department of Genetics at Harvard Medical School invites applicants for a tenure-track faculty position at the rank of Assistant Professor. The Department of Genetics consists of faculty working on diverse problems using a variety of approaches and model organisms, unified in their focus on the genome as an organizing principle for understanding biological phenomena. We are seeking outstanding applicants, with a demonstrated potential for imaginative research and a clear vision for the future, who are working on exciting problems in any area of genetics, broadly defined. The successful candidate is expected to direct innovative and independent research and participate in the teaching of graduate and medical students. Significant scholarly and scientific resources are readily available with this position. Our highly interactive Department provides the opportunity to interact and collaborate with other dedicated researchers within the diverse Harvard research community. For further information about our Department, please see our Web Page: **http://genetics.med.harvard.edu**.

Applicants should submit electronic copies of curriculum vitae, bibliography, a brief description of research accomplishments and future research interests (limit to 500 words) by **October 31, 2010**, and ask three references to provide letters of recommendation. These materials should be sent to the following email address: **faculty_search@genetics.med.harvard.edu**.

We strongly encourage applications from women and minority candidates. Harvard University is an Equal Opportunity/Affirmative Action Employer.

Full Professor in Immunobiology

Wenner-Gren Institute
for Experimental Biology

Stockholm University

The Wenner-Gren Institute for Experimental Biology at Stockholm University invites applicants for a faculty position at the Full Professor level in Immunobiology. We are looking for an outstanding investigator that is contributing to a molecular understanding of fundamental questions in vertebrate immunology. Applicants must have an exceptional record of research productivity and demonstrated scientific proficiency at a high international level with a clearly defined program of independent research.

The position offers significant scientific resources in a stimulating environment. In addition to carrying out research, the incumbent is expected to participate in teaching activities at the University at the undergraduate and post-graduate levels.

For more information, please access the Wenner-Gren Institute webpage: **www.wgi.su.se**. Initial enquires, and requests for additional information may be directed in confidence to Prof. Per O. Ljungdahl,
e-mail: **per.ljungdahl@wgi.su.se.**

Applications must be submitted using the *Template for application for employment and for promotion to the rank of professor or senior lecturer at Stockholm University*. The template and other relevant documents including *Rules of Employment for the hiring of Teachers* can be downloaded from **www.su.se/nyanstallning** or be obtained from the administrative coordinator Katarina Gustafsson,
e-mail: **katarina.gustafsson@science.su.se.**

Applications are welcome quoting ref no **SU 611-0889-10**, and should be received no later than **November 1, 2010.**

Stockholm University is an equal opportunity employer intent on increasing the proportion of women in research and teaching. Female scientists are encouraged to apply.

NUI Galway
OÉ Gaillimh

Applications are invited for the following post:

College of Medicine, Nursing & Health Sciences

Lecturer (Below the Bar) in Pharmacology – Digestive Sciences

Salary: €40,256 p.a. - €56,782 p.a.

Closing Date: Thursday 7th October 2010

Application details/procedure:

For further information and to make an application please visit www.publicjobs.ie

National University of Ireland, Galway is an equal opportunities employer.

publicjobs.ie
An tSeirbhís um Cheapacháin Phoiblí
Public Appointments Service

www.nuigalway.ie

STOWERS INSTITUTE®
FOR MEDICAL RESEARCH

Faculty Search

The Stowers Institute has multiple openings for exceptional scientists interested in applying innovative and/or multidisciplinary approaches to significant and fundamental problems in biology.

Successful candidates will receive substantial ongoing and renewable intramural support, as well as access to extensive core laboratory facilities.

Candidates with Ph.D. or M.D. degrees, postdoctoral research experience, and outstanding records of research accomplishment should send a curriculum vitae and statement of research plans to **facultysearch@stowers.org** by October 31, 2010.

More information may be found at
www.stowers.org

The Stowers Institute is committed to equal opportunity in all its programs.

THE UNIVERSITY of NORTH CAROLINA
GREENSBORO

Assistant Professors of Biology

The Department of Biology at the University of North Carolina - Greensboro (UNCG) invites applications for two tenure-track Assistant Professor positions in Biology. We seek outstanding individuals with research interests in toxicology. These searches are part of an initiative to expand our new doctoral program in Environmental Health Science. Our broadly based doctoral program addresses environmental concerns that directly or indirectly affect human health and well-being from the global to the molecular levels. Therefore, we seek individuals with research interests in environmental toxicology, including at least one person working at the cellular/molecular level. Successful applicants will be expected to develop a strong, externally funded research program, train undergraduate and graduate students, make significant contributions to our Ph. D. program, and teach courses relevant to their specialty. Synergies with faculty in related disciplines are encouraged.

Candidates must hold the Ph.D. by August 1, 2011, and postdoctoral experience is preferred. Applicants should mail a cover letter, CV, brief statements of research goals and teaching philosophies, and arrange for 3 letters of recommendation (e-mail acceptable with hard copy to follow) to be sent to **Ms. Kathe Martin (kamarti3@uncg.edu), Biology Department, UNCG, 312 Eberhart Building, 321 McIver St., Greensboro, NC 27412**. Inquiries should be directed to Dr. E. P. Lacey **(eplacey@uncg.edu)**, Search Committee Chair. The evaluation of applications will begin October 1 and continue until filled. Positions start in August 2011.

UNCG is especially proud of the diversity of its student body, and we seek to attract an equally diverse applicant pool for this position, including women and members of minority groups.

For information about our Ph.D. program, see
http://www.uncg.edu/bio/gradprograms/PhD_Environ_Health_Sci.html.

UNCG is an EEO/AA employer with a strong commitment to increasing faculty diversity.

Chemical Biology/ Medical Research

The OHSU Department of Physiology and Pharmacology invites applications for **tenure-track** faculty positions from individuals with a solid chemistry background interested in applying the tools and techniques of chemistry to biological and biomedical research. We are especially interested in candidates having a strong background in organic synthesis and research interests targeting important areas in biology and medicine.

Preference will be given to candidates for the position of **Assistant Professor,** but exceptional candidates for the position of **Associate** and **Full Professor** will also be considered. We seek individuals who will develop an independent research program, contribute to the teaching of medical and graduate students and interact with investigators studying drug metabolism, signal transduction, ion channel biology, G-protein coupled receptors and cardiovascular and reproductive biology.

OHSU offers a highly interactive research environment and superb opportunities for career development in a spectacular Pacific Northwest setting. A complete application consists of a curriculum vitae, a brief summary of research accomplishments, an outline of future research plans, and three letters of recommendation.

Applications and letters of recommendation may be directed to:
Thomas S. Scanlan, Ph.D.
Professor of Physiology and Pharmacology and
Director, Program in Chemical Biology,
Faculty Search (CB)

Dept. of Physiology and Pharmacology
Mail code L334
Oregon Health & Science University
3181 S.W. Sam Jackson Park Road
Portland OR, 97239-3098

OREGON HEALTH & SCIENCE UNIVERSITY

OHSU is an equal opportunity, affirmative action institution.

ION CHANNEL RESEARCH UNIT
Duke University Medical Center

ICRU

Tenure Track Faculty Position
Assistant Professor/Associate Professor

The Ion Channel Research Unit (ICRU) at Duke University Medical Center invites applications for a tenure track faculty position.

The candidate should be a scientist or a physician-scientist with a laboratory research program in an area of membrane excitability and/or ion channel structure/function and/or ion channel physiology. Among the broad research areas relevant to this search are programs focusing on channelopathies, neuropsychiatric disorders and neuronal function, cardiac arrhythmias, peripheral nociception, optogenetics, structural biology, and development.

The ICRU is a multi-departmental and interdisciplinary group of investigators organized around membrane excitability. The laboratory of the successful applicant will be within ICRU space adjacent to ICRU members and the applicant will receive a primary appointment in an appropriate basic or clinical department within the medical school. Opportunities to interact with and build upon programs relevant to membrane excitability include those in neuroscience, cardiac electrophysiology, structural biology, hormone signaling, renal physiology, and development.

The candidate is expected to work primarily as laboratory researcher. High priority will be placed on creativity in laboratory research, potential for independent funding, and dedication to excellence in teaching. A generous start up package commensurate with the candidate's academic level will be provided. Interested individuals should submit a CV, statement of research interest, and request that three letters of references to be sent as PDF files directly to: **icru@mc.duke.edu**. The deadline for receipt of applications is **November 22, 2010**.

Duke University Medical Center is an Equal Opportunity/Affirmative Action Employer.

UMASS AMHERST

Assistant Professor Tenure-Track

Computational Biology or Bioinformatics
Department of Computer Science

We invite applications from Ph.D.-level computer scientists for a Five College joint faculty position based at UMass Amherst with research, teaching, and service shared with Mount Holyoke College, providing the successful candidate with the unique opportunities of both a premier research university and an elite liberal arts college. For details on the Five College Consortium, visit: www.fivecolleges.edu. Focus areas could include proteomics, metabolomics, genomics, systems biology, statistical genetics, evolutionary biology, medical informatics, or other areas at the intersection of computer science, biology, and biotechnology. The successful candidate will enjoy exciting opportunities for collaboration in such research areas as protein folding, genome sequence annotation, imaging, machine learning, and cellular biophysics. Teaching and post-doctoral experience preferred. UMass Amherst and Mount Holyoke College are strongly committed to having a diverse faculty and student body. For more information, visit: www.cs.umass.edu/bioinfosearch.

Send curriculum vitae, a description of research interests and teaching experience, and three letters of recommendation to: Chair, Bioinformatics Search Committee, Computer Science Department, 140 Governors Drive, UMass Amherst, Amherst, MA 01003-9264; electronic submissions are encouraged: bioinfosearch@cs.umass.edu. Review of applications will begin November 15, 2010, and continue until the position is filled.

The University of Massachusetts is an Affirmative Action/ Equal Opportunity Employer. Women and members of minority groups are encouraged to apply.

University of Pittsburgh
School of Medicine

Cell Biology Faculty Positions

The Department of Cell Biology and Physiology at the University of Pittsburgh, School of Medicine seeks candidates for Assistant, Associate and/or Full Professor tenure stream and tenured faculty positions. Successful candidates will be expected to establish and maintain a vigorous, innovative and independent research program in the broad area of cell biology, including, but not limited to organelle dynamics and biogenesis, membrane trafficking, intracellular signaling, cytoskeleton, autophagy and systems biology aimed at basic cell biology questions The successful candidate will join an interactive, interdisciplinary group of faculty, students and fellows, and enjoy access to the state-of-the-art equipment and facilities at the University of Pittsburgh. Candidates must hold a Ph.D. or an equivalent degree and have a strong record of research accomplishments. Highly competitive start-up, compensation and benefits packages are offered.

Curriculum vitae, statement of research interests, two recent most important papers, and e-mail addresses of three references can be sent to: **cbprecru@pitt.edu**. Review of applications will begin immediately and continue until the positions are filled.

The University of Pittsburgh is an Equal Opportunity/Affirmative Action Employer.

NEUROSCIENCE AND CELL BIOLOGY

The Department of Neuroscience and Cell Biology at UMDNJ-Robert Wood Johnson Medical School seeks a full-time faculty member at any academic level whose primary responsibility will be to develop and direct a new Neuron, Brain and Behavior course as part of a multidisciplinary, integrated medical curriculum. Additional responsibilities will include developing and directing Neuroscience courses for Physician Assistant students and Masters level graduate students as well as contributing neuroscience expertise to the Medical Gross Anatomy curriculum. Experience in medical education, in particular case based learning and other innovative educational methods, is highly desired.

To apply please send a Teaching Portfolio including a short statement of teaching philosophy, a Curriculum Vitae and 3 letters of recommendation to: **Dr. Cheryl Dreyfus, Professor and Acting Chair, Department of Neuroscience and Cell Biology, UMDNJ-Robert Wood Johnson Medical School, 675 Hoes Lane, Piscataway, NJ 08854, Attn. Ms. Beth Sparta**. UMDNJ is an Affirmative Action/Equal Opportunity Employer, m/f/d/v, and a member of the University Health System of New Jersey.

UMDNJ
ROBERT WOOD JOHNSON MEDICAL SCHOOL
University of Medicine & Dentistry of New Jersey

Virginia Tech
Invent the Future

College of Science
Cluster Hires

The College of Science at Virginia Tech, in support of the university's strategic plan, is expanding its research presence in: **Energy and the Environment, Earth Systems, Neuroscience, Infectious Diseases, and Visualization and Pattern Recognition**. Faculty members will be recruited across several colleges to promote research efforts in these areas. Subject to budgetary approval, we intend to recruit new faculty in Biological Sciences, Chemistry, Economics, Geosciences, Mathematics, Physics, Psychology, and Statistics within the College of Science.

Both junior and senior level candidates are encouraged to apply. Please visit **www.science.vt.edu** and click on the links under Faculty Openings. Consideration of applications will begin as early as **October 15, 2010** and will continue until the positions are filled.

Virginia Tech is an AA/EEO employer; applications from members of underrepresented groups are especially encouraged.

College of Science
Biological Sciences • Chemistry • Economics
• Geosciences Mathematics • Physics • Psychology
• Statistics

VCU Medical Center

FACULTY POSITIONS IN HEPATOBILIARY/PANCREATIC DUCT CANCER RESEARCH

As part of its new major strategic research plan, Virginia Commonwealth University's School of Medicine in conjunction with the VCU Massey Cancer Center, a NCI-designated cancer center, is seeking applicants for two full-time tenure-track faculty positions at the Assistant, Associate, or Full Professor rank to join an expanding basic and translational research initiative with a focus on the molecular pathology and target-based therapeutics of hepatobiliary and pancreatic duct cancers.

Successful candidates should possess outstanding research credentials that complement and extend our current areas of research strengths, including those focused on model systems of hepatobiliary cancer development and progression, molecular pathology and pathogenesis of cholangiocarcinoma, bile acid signaling and growth factor receptor tyrosine kinases, tumor microenvironment, and target-based cancer therapeutics. Preference will be given to candidates who have transferable NIH-R01 funding or who are likely able to successfully compete for such funding. Selected candidates will also be expected to meet institutional requirements for participating in graduate student and postdoctoral training. Individual faculty appointments will be made in appropriate basic science or clinical departments, with academic rank based on the applicant's qualifications. Successful candidates will receive a very generous start-up package, together with a competitive salary and excellent research space situated to maximize collaborative interactions. Candidates must have an earned M.D., Ph.D., or M.D./Ph.D. and demonstrate research accomplishments in the field of hepatobiliary and/or pancreatic duct cancer.

Interested individuals should submit a curriculum vitae, a summary of research interests and plans, and contact information and e-mail addresses for three professional references to: Dr. Alphonse E. Sirica, Search Committee Chair, Department of Pathology, Virginia Commonwealth University School of Medicine, P.O. Box 980297, Richmond, Virginia 23298-0297 at asirica@mcvh-vcu.edu.

Virginia Commonwealth University is an Equal Opportunity/Affirmative Action Employer. Women and minorities are encouraged to apply.

MICHIGAN STATE
UNIVERSITY

Microbial Pathogenesis
Department of Microbiology and Molecular Genetics

The Department of Microbiology and Molecular Genetics at Michigan State University seeks candidates for a position at the Assistant, Associate or Full Professor level in microbial pathogenesis. Applicants are sought with demonstrated expertise in molecular mechanisms of pathogenesis, the evolution of pathogenicity, bacterial pathogenesis, microbial ecology of infectious diseases, genetics of virulence, or host immune-microbe interactions. Many opportunities exist for collaboration with other faculty in newly funded centers including a NSF STC center for the study of evolution in action (BEACON) and a NIH Enteric Research Investigational Network. Additional collaborative groups include the Center for Microbial Pathogenesis, Center for Microbial Ecology, and the Center for Water Sciences. The person who fills this position will be expected to build and lead collaborative groups. Expectations include a strong record of research accomplishment and, depending on rank, an independent, externally funded research program with broad visibility. Teaching within our graduate, professional, and/or undergraduate programs is anticipated. The offer will include a competitive startup package and laboratory facility. Applicants should submit a letter of application, curriculum vitae, history of funding, statement of future research plans, and contact information for three referees (address, e-mail and phone) to **mmgchair@msu.edu** or to:

Microbial Pathogenesis Search Committee Chair
Dept of Microbiology and Molecular Genetics
2209 Biomedical & Physical Sciences Building
Michigan State University, East Lansing, MI 48824
mmgchair@msu.edu

We will begin review applications in October and applications will be accepted until the position is filled.

Michigan State University is an Equal Opportunity Employer. Women and minority candidates are encouraged to apply.

Faculty Position
Structural Biology Program
Sloan-Kettering Institute

The Structural Biology Program of the Sloan-Kettering Institute (www.ski.edu) invites applications for a tenure-track faculty position at the Assistant Member level (equivalent to Assistant Professor). We are interested in outstanding individuals who have demonstrated records of significant accomplishment. Areas of interest include x-ray crystallography, NMR spectroscopy, EM and optical imaging, as well as the interface of structural, chemical and computational biology. Faculty will be eligible to hold graduate school appointments in the Gerstner Sloan-Kettering Graduate School of Biomedical Sciences, the Weill Cornell Graduate School of Medical Sciences, as well as the Tri-Institutional MD/PhD Training Program.

The deadline for applications is **November 1, 2010**. Interested candidates should visit **http://facultysearch.ski.edu** to apply via the on-line faculty application. Informal inquiries may be sent to **Julie Kwan at kwanj@mskcc.org** or to **Dr. Nikola Pavletich, Chair, Structural Biology Program at palvletin@mskcc.org**. MSKCC is an equal opportunity and affirmative action employer committed to diversity and inclusion in all aspects of recruiting and employment. All qualified individuals are encouraged to apply.

Memorial Sloan-Kettering Cancer Center
www.mskcc.org

ENDOWED CHAIR IN MACROMOLECULAR STRUCTURE AND FUNCTION

The Ohio State University

The Departments of Biochemistry and Chemistry at The Ohio State University seek applications to fill the faculty position of **OHIO EMINENT SCHOLAR**, a fully endowed tenured faculty position. The successful applicant will have well-documented research qualifications using modern analytical and physical approaches to investigate topics at the forefront of macromolecular structure and function. Individuals with research interests in proteomics, structure determination, molecular recognition and targeting, epigenetics, RNA biology, metabolomics, or other generally related areas are encouraged to apply. However, more than the specific focus, the quality of the applicant's research program and promise for future accomplishments will be of primary importance. The successful applicant will be provided with a competitive salary, ample laboratory space, generous start-up funding for equipment and personnel, and an on-going annual operating budget.

The Departments of Biochemistry and Chemistry consist of ~55 faculty members, many of whom are actively engaged in the general research area of macromolecular structure and function, affording many opportunities for productive interactions and collaborations with the successful candidate. General information about the University and the Columbus metropolis is available through links at: http://www.osu.edu.

Informal enquiries from potential applicants are strongly encouraged. Contact Prof. Richard P. Swenson (swenson.1@osu.edu; telephone: 614-292-9428) for further information. A curriculum vitae, description of research experience and future plans can be sent by email to the above address or the **Eminent Scholar Search Committee, Attn: R.P. Swenson, Dept. of Biochemistry, The Ohio State University, 484 West 12th Ave, Columbus, Ohio 43210.** Review of applications will begin immediately and continue until the position is filled.

To build a diverse workforce, Ohio State encourages applications from individuals with disabilities, minorities, veterans, and women.

The Ohio State University is an EEO/AA and NSF ADVANCE employer

Assistant Professor Position
Department of Molecular and Cellular Biology
and
FAS Center for Systems Biology
Harvard University

We seek applications for a tenure-track faculty position in the fields of molecular and cellular biology and biochemistry. We are particularly interested in candidates who take systems biological approaches to address fundamental questions in biology. The Department and Center cover a broad range of topics, including molecular biology, genetics, cell biology, systems biology, developmental biology, neurobiology, computational biology, molecular evolution, theoretical biology, biochemistry, and structural biology, and provide access to state of the art animal facilities and core facilities (imaging, proteomics, genomics, bioinformatics). The Department and Center are closely associated with science initiatives at Harvard such as the Center for Brain Science, the Harvard Stem Cell Institute, the Broad Institute, and the Center for Nanoscale Systems.

We strongly encourage applications from women and minority candidates. Applications should include: curriculum vitae, reprints of publications, and a statement of present and future research plans (1-3 pages). Complete applications and three letters of recommendation, solicited by the applicant, should be receive not later than **3 November 2010**.

Submit application to: **http://www.mcb.harvard.edu/Jobs/Faculty**

For information contact **Kimberly Kriz**, **kkriz@mcb.harvard.edu**, Department of Molecular and Cellular Biology, Harvard University.

Harvard is an Affirmative Action/Equal Opportunity Employer.

www.mcb.harvard.edu
http://sysbio.harvard.edu/csb/

COLUMBIA UNIVERSITY
College of Physicians and Surgeons

Physician-Scientist Faculty Position in Immunology and Pediatrics

The Department of Microbiology & Immunology and the Department of Pediatrics at Columbia University, College of Physicians and Surgeons, are jointly recruiting a physician-scientist/immunologist whose research impacts pediatrics (e.g., IBD, allergy, autoimmunity, vaccine biology). We seek outstanding candidates pursuing basic and/or translational research in immunology who will foster broader collaborations between our departments. Rank may range from tenure-eligible assistant professor to full professor with tenure. Candidates must hold M.D. or M.D./Ph.D. degrees or equivalent and will be expected to maintain or develop an independent research program and participate in departmental teaching. Clinical service is not required but may be arranged if desired. A competitive recruitment package, including housing assistance, will be provided. For further information about the Department of Microbiology & Immunology and Columbia University Medical Center, please visit: http://www.microbiology.columbia.edu.

For information about immunology research in the Department of Pediatrics, please visit: http://www.cumc.columbia.edu/dept/pediatrics/allergy/immunology_research_intro.html.

Please submit current curriculum vitae, a two- to three-page summary of present and future research interests, and three letters of recommendation. The online application is available at

https://academicjobs.columbia.edu/applicants/Central?quickFind=53596 for both submission and further information about this posting. Review of applications will begin immediately and continue until the position is filled.

Columbia University is an equal opportunity/affirmative action employer.

Two Faculty Positions in Microbiology
Assistant Professor and Open Rank
Indiana University, Bloomington

The Indiana University Department of Biology (**http://www.bio.indiana.edu**) Microbiology Section (**http://www.bio.indiana.edu/graduate/micro/faculty.php**) invites applications for two faculty positions. One position is tenure-track at the Assistant Professor level and the other position is open to all faculty ranks, including senior candidates. The successful candidates will be provided with a competitive startup package and salary, and will have access to outstanding research resources. Successful junior level candidates will be expected to develop a vigorous externally funded research program. Senior-level candidates are expected to be leaders in their field of research as demonstrated by strong publication and funding records. Both successful candidates will participate in teaching at the undergraduate and graduate levels. We are particularly interested in microbiologists whose research focuses on (i) environmental, genomic, and/or systems microbiology, and (ii) fundamental bacterial mechanisms in all areas including phage and pathogen models.

Applications received by **October 15, 2010** will be assured of full consideration. Inquiries should be sent to **Yves Brun** at **iumicro@indiana.edu**. Applicants should send a single PDF file that contains a cover letter, CV, research (past, present, and planned) and a teaching statement by E-mail to the above address and/or mail materials to **Microbiology Search Committee c/o Yves Brun, Department of Biology, Indiana University Bloomington, Jordan Hall, Room 142, Bloomington, IN 47405**. Please arrange to have at least four letters of recommendation sent by E-mail to the above address.

Indiana University is an Affirmative Action/Equal Opportunity Employer. Women, minority candidates, and couples are encouraged to apply.

UNIVERSITY OF UTAH SCHOOL OF MEDICINE

A tenure track appointment is available in the Department of Biochemistry for autumn 2011. Areas of emphasis include protein and nucleic acids biochemistry, cellular function, metabolism, enzymology, signal transduction, and computational analysis. Preference will be given to applicants at the Assistant Professor level. A doctoral degree and strong record of research accomplishment are required. The successful candidate will join an interactive and diverse faculty, and will participate in campus-wide graduate training programs. Deadline for applications is **November 15, 2010**; late applications will be considered if an opening is still available.

Apply online at:
http://www.biochem.utah.edu/facultysearch/

The University of Utah is an Affirmative Action/Equal Opportunity employer and does not discriminate based upon race, national origin, color, religion, sex, age, sexual orientation, gender identity/expression, disability, or status as a Protected Veteran. Upon request, reasonable accommodations in the application process will be provided to individuals with disabilities. To inquire about the University's nondiscrimination policy or to request disability accommodation, please contact: Director, Office of Equal Opportunity and Affirmative Action, 201 S. Presidents Circle, Rm. 135, (801)581-8365.

THE UNIVERSITY of WISCONSIN MADISON

FACULTY POSITION IN VETERINARY ONCOLOGY

The Department of Medical Sciences, School of Veterinary Medicine, University of Wisconsin Madison seeks candidates for the Barbara A. Suran Endowed Chair tenure track faculty position in Veterinary and Comparative Oncology at the rank Associate or Full Professor.

Candidates should possess a DVM (or professional equivalent) degree and a record of excellent independent scholarship in basic or clinical research in Veterinary and/or Comparative Oncology. A Ph.D and/or Board certification by the American College of Veterinary Internal Medicine (Oncology) is desired, but not required. Applicants must have demonstrated a strong commitment to the education of professional students, graduate students, and residents through a history of high quality instruction and service.

The successful candidate will direct independent research in the field of comparative oncology through the administration of the Barbara A. Suran Fund for Oncology Medical Science Research Excellence (Endowed) under the umbrella of the Barbara A. Suran Oncology Research Institute located within the School of Veterinary Medicine. Also, the successful candidate will engage graduate students, residents and veterinary students in classroom and laboratory teaching, and clinical service that advances the mission of the School. Distribution of effort will be 60% research, 30% instruction/clinical service, and 10% university service.

The Department fosters a multidisciplinary approach to research. Ongoing areas of research include comparative oncology, investigational comparative cancer clinical trials through the inclusion of companion animals with cancer, and pharmacogenomics. Established and emerging strengths include explorations of novel chemotherapy and immunotherapy modalities, the comparative relevance, and investigation of molecular, and functional imaging modalities to better inform the delivery of conformal radiation therapy (e.g., onsite TomoTherapyTM). Additionally, through institutional partnerships with the NIH/NCI-designated Carbone Comprehensive Cancer Center, significant collaborative activities are available and expected. Rank and salary will depend on experience and qualifications. Deadline for receipt of application and reference letters is **October 31, 2010** or until a suitable candidate is identified. Applicants cannot be guaranteed confidentiality.

Applicants are invited to submit a curriculum vitae, letter of intent summarizing career goals and current activities, and names and addresses of three references to: **Dr. Mark D. Markel, Chair, Department of Medical Sciences, School of Veterinary Medicine, University of Wisconsin Madison, 2015 Linden Drive, Madison, WI 53706-1102**. Informal inquiries maybe directed to **Dr. David Vail** (Chair of Search Committee) at **608-890-1324** or e-mail **vaild@vetmed.wisc.edu**.

The University of Wisconsin is an Affirmative Action Equal Opportunity Employer committed to diversity.

VANDERBILT UNIVERSITY

FACULTY POSITION
DEVELOPMENTAL GENETICS

The Department of Biological Sciences at Vanderbilt University seeks a developmental geneticist using zebrafish as the experimental system to fill a tenured faculty position at the associate or full professor rank. We desire candidates whose research broadly overlaps and complements existing areas of interest within the department (**http://sitemason.vanderbilt.edu/biosci**). For information about developmental biology at Vanderbilt, see **http://www.mc.vanderbilt.edu/devbio/**. The central criteria for the position are excellence in research and the ability to teach undergraduate and graduate students with a high level of effectiveness.

Applicants should send a PDF containing a letter of application, curriculum vitae, and a statement of current and future research interests to **sheri.m.stephens@vanderbilt.edu**. Applicants also should arrange for three letters of recommendation to be sent to the same email address. Review of applicants will begin **November 1, 2010**, and will continue until the position has been filled.

Vanderbilt University is an Affirmative Action/Equal Opportunity Employer. Women and under-represented minority candidates are especially encouraged to apply.

The UC Davis Genome Center integrates experimental and computational approaches to address key problems at the forefront of genomics. The Center is housed in a new research building with state-of-the-art computational and laboratory facilities and currently comprises 15 experimental and computational faculty. These faculty are part of an internationally recognized program in genomics and computational biology at Davis, building on and enhancing the unique strengths and unmatched breadth of the life sciences on the UC Davis campus.

The Genome Center and the School of Medicine invites applications for a tenure-track faculty position in the area of human genetics and genomics. Applicants interested in genomic approaches to human diseases and investigators employing large-scale, technology-driven approaches that complement existing strengths at UC Davis are particularly encouraged to apply. Candidates should be strongly motivated by the biological and medical importance of their research and should value the opportunity to work in close collaboration with other groups and disciplines.

Candidates may be at any academic level. At the senior level, we invite applications from prominent scientists with distinguished records of research, teaching, and leadership in genomics. At the junior level, we invite applications from candidates whose accomplishments in innovative research and commitments to teaching demonstrate their potential to develop into the future leaders in human genetics and genomics.

This position requires a Ph.D. or equivalent. The appointment will be at the Assistant, Associate or Full Professor level in an appropriate academic department in the School of Medicine. The position will remain open until filled. For fullest consideration, applicants should submit a letter of application, a curriculum vitae, statements of research and teaching interests, and the names of at least five references to the Genome Center Web site **http://genomecenter.ucdavis.edu** by **November 1, 2010**.

The University of California is an Affirmative Action/Equal Opportunity Employer.

HUNTSMAN CANCER INSTITUTE UNIVERSITY OF UTAH

UNIVERSITY OF UTAH HEALTH SCIENCES

The **Department of Radiation Oncology** and the **Huntsman Cancer Institute** invite applications for a tenure-track faculty position in the general field of molecular radiobiology. We seek a basic scientist with a PhD or MD/PhD with a track record of scientific excellence and potential to lead an NCI-funded research program. We prefer candidates at the **Assistant** or **Associate Professor** level. Research interest is broadly defined and includes investigation of basic cellular mechanisms altered in cancer, tumor models and translational research. The candidate also will contribute to the teaching of radiobiology to Radiation Oncology Residents. For those with MD/PhD qualifications in Radiation Oncology, we offer a part-time clinical position with protected research time. We offer strong institutional support, state-of-the-art laboratory and core facilities, a collegial and interactive research environment that fosters the development of junior faculty and robust graduate programs for training PhD and MD/PhD students.

Candidates are encouraged to apply by **January 1, 2011**, with their curriculum vitae, a description of research interests and accomplishments and three letters of recommendation to:

Huntsman Cancer Institute, University of Utah
Attn: Recruitment Office, Room 5363
2000 Circle of Hope, Salt Lake City, UT 84112-5550
e-mail: hci.recruitment@hci.utah.edu

The University of Utah is an Affirmative Action/Equal Opportunity employer and does not discriminate based upon race, national origin, color, religion, sex, age, sexual orientation, gender identity/expression, disability, or status as a Protected Veteran. Upon request, reasonable accommodations in the application process will be provided to individuals with disabilities.

To inquire about the University's nondiscrimination policy or to request disability accommodation, please contact: Director, Office of Equal Opportunity and Affirmative Action, 201 S. Presidents Circle, Rm 135, Salt Lake City, UT 84112 801-581-8365.

The University of Texas at Austin

Virology Position

The Institute for Cellular and Molecular Biology

The Section of Molecular Genetics and Microbiology at the University of Texas at Austin invites applicants for a tenure-track faculty position in virology at the Assistant Professor level. Outstanding applicants at the rank of tenured Associate or Full Professor will also be considered. Candidates should have an outstanding record of research productivity and a well-conceived research plan. We are particularly interested in candidates studying the molecular biology of replication and gene expression of animal viruses, virus-host interactions, innate immunity and viral pathogenesis. We seek an investigator who will build an active, funded research program and will teach effectively at the undergraduate and graduate levels. The successful candidate will be eligible for membership in the Institute for Cellular and Molecular Biology, will have access to its extensive core facilities, and will have the opportunity to participate in several graduate programs. The position offers excellent start-up funds, salary and laboratory space in a new building that is part of a dynamic, highly interactive research environment.

Please send a single PDF file containing your curriculum vitae, summary of research interests, and names of three references before December 1, 2010 to: **mgm_search@biosci.utexas.edu**. References should also send their letters directly to the same email address prior to December 1, 2010.

Homepages • http://www.biosci.utexas.edu/mgm/ • http://www.icmb.utexas.edu

The University of Texas at Austin is an Equal Opportunity Employer. Qualified women and minorities are encouraged to apply; a background check will be conducted on applicant selected.

CETI Center for Evolutionary and Theoretical Immunology
University of New Mexico • Los Alamos National Laboratory • Santa Fe Institute

VERTEBRATE EVOLUTIONARY IMMUNOLOGIST DEPARTMENT OF BIOLOGY, UNIVERSITY OF NEW MEXICO CENTER FOR EVOLUTIONARY AND THEORETICAL IMMUNOLOGY (CETI)

The Biology Department at the University of New Mexico is seeking applications for an Assistant Professor in the area of **evolutionary/comparative vertebrate immunology**. This position is full-time, tenure-track, and is funded, in part, by an NIH Center of Biomedical Research Excellence (COBRE) award that supports the Center for Evolutionary and Theoretical Immunology (**http://ceti.unm.edu**).

We seek a colleague who will establish and maintain a vigorous, independent research program, is committed to excellence in teaching at the undergraduate through graduate levels, and is interested in joining a broadly based Biology Department.

Applicants must have a Ph.D. in biology or a related discipline at the time of appointment. Relevant postdoctoral experience preferred. Applicants must submit a cover letter, curriculum vitae, three representative reprints, and statements of current and future research and teaching interests. All application material must be uploaded and submitted through UNM's electronic application system, **UNMjobs, https://unmjobs.unm.edu**. Applicants must also arrange for at least three letters of reference to be sent directly to **biohire@unm.edu**. Application materials must be received by close of business day, **October 29, 2010**, for best consideration.

Questions related to this posting may be directed to **Dr. Charles Cunningham, ccunnin@unm.edu**.

The University of New Mexico is an Equal Opportunity/Affirmative Action Employer and Educator. Women and underrepresented minorities are encouraged to apply.

Santa Clara University
Assistant Professor of Bioengineering

The Bioengineering Program at Santa Clara University (SCU) is undergoing a rapid phase of expansion. As part of this growth, the School of Engineering at SCU invites applications for a tenure-track faculty position at the Assistant Professor level. Candidates with a Ph.D. and demonstrated achievement in research and strong interest in teaching in all areas of Bioengineering are encouraged to apply. Particular areas of specialization include, but are not limited to tissue engineering, biomaterials and biomolecular engineering.

SCU is committed to learning, scholarship, and engagement with society. All candidates are expected to commit to undergraduate and graduate teaching and to develop an active and externally funded research program. Our location in the heart of Silicon Valley facilitates collaborations with established and emerging companies and with other research institutions.

Interested candidates should submit a letter of application, a detailed CV, a statement of professional interests, and contact information for three references. The application can be submitted electronically to **bioengineering@scu.edu** (preferred) or by mail to: **Chair, Bioengineering Search Committee, College of Engineering, Santa Clara University, 500 El Camino Real, Santa Clara, CA 95053**. Consideration of applications will begin on **November 15, 2010**, and the position will remain open until filled.

Santa Clara University is an Equal Opportunity/Affirmative Action Employer, and welcomes applications from women, persons of color, and members of other historically underrepresented U.S. ethnic groups.

Deputy Director

National Human Genome Research Institute

The National Human Genome Research Institute (NHGRI), a major research component of the National Institutes of Health (NIH) and the Department of Health and Human Services (DHHS), seeks to identify an outstanding Deputy Director.

The NHGRI Deputy Director will assist the Director in providing overall leadership of the Institute, sharing responsibilities in all phases of leading the preeminent organization dedicated to advancing genomic and genetic research, including its clinical applications. As a member of the NHGRI senior leadership, the Deputy Director will work with the Director in shaping and executing a strategic vision for the Institute as well as communicating that vision to the Institute staff and the broader scientific community. In working closely with the Director, the Deputy Director helps to develop Institute goals, priorities, policies, and program activities; this requires staying abreast of developments and needs of the Institute and the field.

Applicants must have an M.D. and/or Ph.D or equivalent degree in the biomedical sciences, as well as a broad knowledge of the field of human genetics and genomics. They must further have a compelling vision for the future of the field and the role for NHGRI within the field. Also required are senior-level research and/or clinical experience and knowledge of the major scientific areas related to genetics and genomics, in addition to well-honed administrative and interpersonal skills to meet the demands of helping to lead a complex organization. Applicants should have demonstrated leadership in dealing with different stakeholder groups within the research community, planning and assessing programs, developing plans to resolve operational problems and issues, and managing financial and human resources. Applicants should be known and respected within their profession, both nationally and internationally as individuals of outstanding scientific competence.

Salary is competitive and will be commensurate with the candidate's experience. A full Federal benefit package is available, including retirement, health and life insurance, long-term care insurance, annual and sick leave, and the Thrift Savings Plan (401K equivalent).

Interested applicants should submit a cover letter that includes a brief description of research, clinical, and/or administrative experience, a current curriculum vitae and bibliography, names and contact information of five references, and a brief written vision for becoming the NHGRI Deputy Director. Questions about the position and applications themselves should be sent to Ms. Ellen Rolfes via email at ellenr@exchange.nih.gov. All information provided by the candidates will remain confidential and will not be released outside the NHGRI search process without a signed release from the candidate.

Applications will be reviewed starting November 1, 2010, and will be accepted until the position is filled.

DHHS and NIH are Equal Opportunity Employers and encourage applications from women and minorities.

NATIONAL HUMAN GENOME RESEARCH INSTITUTE
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES | NATIONAL INSTITUTES OF HEALTH | genome.gov

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National Eye Institute

Vacancy Announcement
Tenure Track Position in The Office of the Scientific Director
National Eye Institute (NEI)
National Institutes of Health (NIH)
Department of Health and Human Services (DHHS)

The National Eye Institute (NEI), Office of the Scientific Director, seeks an outstanding clinician-scientist for a tenure-track position to develop an independent translational research program with focus on retinal diseases.

The candidate will examine and treat patients with ophthalmic disease, and conduct clinical trials. NEI has particular interest in clinical research related to neuronal-glial interactions in retinal diseases and to genetic retinal degenerative diseases.

The candidate must hold an M.D. or M.D./Ph.D. degree from a school in the US or Canada, or an equivalent degree from a foreign medical school. Candidates must be Board-certified by the American Board of Ophthalmology or Board-eligible and are expected to have completed post-residency fellowship training in Medical or Surgical Retina.

Salary is commensurate with research experience and accomplishments. A full Federal package of benefits is available (including retirement, health, life and long term care insurance, Thrift Savings Plan etc).

This position will remain open until filled. Interested applicants should submit an electronic application including curriculum vitae, a detailed statement of the proposed research, copies of their five most significant publications, and the names of three references to **Ms. Mica Gordon at gordonmi@nei.nih.gov**

NIH Intramural Research Program is Recruiting "Earl Stadtman Investigators"

We are actively searching for outstanding neuroscientists

The National Institutes of Health is pleased to announce a new call for top-tier tenure-track candidates to become "NIH Earl Stadtman Investigators." This is an opportunity to explore the limits of your productivity and your independence from preconceived research objectives.

NINDS, NIMH, NIDCD, NIDA, NICHD, NEI, NIAAA, NIDCR, NHGRI and NIA together form one of the largest and most active neuroscience communities in the world. With phase two of the Porter Neuroscience Research Center on the NIH Bethesda campus slated for completion in 2013 this community of researchers will become increasingly integrated in this state-of-the-art research facility. Some of the Institutes with neuroscience programs are actively searching for outstanding neuroscientists. We encourage tenure track candidates to apply to the NIH "Earl Stadtman Investigators" search.

Join the NIH team of nearly 1,200 principal investigators and 4,000 trainees. Among us are world-renowned experts in immunology, cancer and rare diseases, to name but a few scientific areas. Our program also includes the NIH Clinical Center, the world's largest hospital entirely devoted to biomedical research. Our strength is our diversity in pursuit of a common goal, to alleviate human suffering.

Qualifications/eligibility: Candidates must have an M.D., Ph.D., D.D.S./D.M.D., D.V.M, D.O., R.N./Ph.D., or equivalent doctoral degree and have an outstanding record of research accomplishments as evidenced by publications in major peer-reviewed journals. Preference will be given to applicants who are in the early stages of their research careers; only non-tenured applicants will be considered. Candidates in any area of basic, translational and clinical neuroscience research are invited to apply. Appointees may be U.S. citizens, resident aliens or non-resident aliens with, or eligible to obtain, a valid employment-authorization visa.

How to apply: Complete applications must be received by October 1, 2010. Interested applicants must submit a curriculum vitae, a three-page research plan, a one-page description of their vision for their future research and its potential impact, and contact information for three professional references through our online application system at http://tenuretrack.nih.gov/apply. Letters of recommendation will be requested automatically when you submit your application. No paper applications will be accepted. More information about the Stadtman Investigator search is at http://tenuretrack.nih.gov.

The European Commission is recruiting the

DIRECTOR-GENERAL OF THE JOINT RESEARCH CENTRE (GRADE AD 15) COM/2010/10279

The Joint Research Centre (JRC) provides robust scientific and technical advice to European policy-makers. It comprises seven research institutes located in five European countries. Operating from the Brussels headquarters, you will oversee a staff of 2750 and an operating budget of €340 million per annum, while driving forward research supporting a competitive economy, low carbon solutions, the sustainable management of natural resources, the safety of food and consumer products, nuclear safety and security, security and crisis management, and reference materials and measurements.

To take on this exceptionally high profile position, you must be able to develop and implement far-reaching strategies and promote excellent relationships with influential stakeholders. This will demand an extensive track record in senior management, including direct responsibility for significant teams and budgets. You will have earned scientific reputation in managing a major research institute or similar scientific body, and have a PhD or equivalent experience in a discipline of relevance to the JRC. Naturally, you will be versed in relevant European Union policies, capable of taking strategic decisions and ready to do whatever it takes to build on the JRC's strong reputation among the scientific and policy communities. Finally, you should be fully fluent in English and familiar with at least one other major European language.

A full job description with the exact eligibility and selection criteria as well as application details can be found in Official Journal C 238 A of 3rd September 2010 or on the EUROPA Website:

http://ec.europa.eu/dgs/human-resources/working_senior_mgt_en.htm

If you want to apply, you must register via the Internet by going to the website:

https://ec.europa.eu/dgs/human-resources/seniormanagementvacancies/

The closing date for registration is 1/10/2010. On-line registration will not be possible after 12.00 noon Brussels time.

eu careers

http://www.ec.europa.eu

EUROPEAN COMMISSION

FACULTY POSITIONS

TENURE-TRACK FACULTY POSITIONS DEPARTMENT OF NEUROSCIENCE SCHOOL OF ARTS AND SCIENCES UNIVERSITY OF PITTSBURGH

Applications are invited for tenure-track positions at the level of Assistant Professor starting September, 2011, pending budgetary approval. Individuals whose research is in the area of molecular and cellular neuroscience are especially encouraged to apply, though other areas will be considered as well. Collegial interactions and collaborative research are widespread within the Department of Neuroscience (**http://www.neuroscience. pitt.edu/**), and across the extensive neuroscience community found in Pittsburgh. Our integrative research environment is exemplified by the Center for Neuroscience at the University of Pittsburgh (CNUP; **http://cnup.neurobio.pitt.edu/**) and the Center for the Neural Basis of Cognition (CNBC; **http://www.cnbc.cmu.edu/**). The successful candidate will be expected to establish an independent research program and participate in teaching neuroscience to undergraduate and graduate students.

Applicants should send electronic copies of curriculum vitae, a brief statement of research accomplishments and goals and contact information for three references, via email to: **nrosci1@pitt.edu**. For full consideration, application materials must be received by **November 1, 2010**. Review of applications will continue until the position is filled.

The University of Pittsburgh is an Affirmative Action, Equal Opportunity Employer. Women and members of minority groups under-represented in academia are especially encouraged to apply.

DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research

Director, Division of Bacterial, Parasitic and Allergenic Products

The Department of Health and Human Services, Food and Drug Administration, Office of Vaccines Research and Review (OVRR), is searching for a Director for the Division of Bacterial, Parasitic and Allergenic Products (DBPAP). The OVRR regulates and performs mission-related research on vaccines and allergenic products to ensure that they are pure, safe and effective. The DBPAP Director leads a dynamic organization of highly skilled, laboratory-based review scientists and support personnel committed to improving access to vaccines and related products through the development of sound science-based policy, effective regulatory processes and application of quality management principles.

Full details and application instructions can be found at **www.fda.gov/AboutFDA/CentersOffices/CBER/ucm223900.htm**.

The Department of Health and Human Services is an Equal Opportunity Employer with a smoke free environment.

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ScienceCareers.org/booklets

Science Careers
From the journal Science AAAS

Veterans Health Administration
Research & Development
Improving Veterans' Lives — www.research.va.gov

Director, Rehabilitation Research and Development Service

The Department of Veterans Affairs (VA) Rehabilitation Research & Development (RR&D) Service seeks qualified candidates for the position of Director.

The goal of RR&D is to improve quality of life of Veterans and their families through restoration of physical, psychological, social, and vocational functions. RR&D integrates multiple scientific disciplines to investigate and develop concepts, processes, and products to directly meet the needs of Veterans with chronic disabling diseases and conditions. Emphasized research areas include neurosciences, aging and neurodegenerative diseases, brain and spinal cord injury, musculoskeletal rehabilitation, rehabilitation engineering, prosthetics, psychological health, social reintegration, sensory systems, and regenerative medicine. The RR&D Service portfolio emphasizes basic research to repair injured organs and tissues; translational research to bring basic discoveries to clinical use; prosthetics, orthotics, and assistive device research; and research aimed at restoring physiological function and social integration.

The Director serves as functional leader and directs, plans, and manages ongoing operations of RR&D to generate new scientific knowledge and provide strategic direction for rehabilitation research.

Candidates must be a United States citizen & possess an M.D. or O.D.

Location: Washington, DC; Salary range: 110,000 to 230,000 USD/yr, determined by compensation panel.

For more information, go to:
http://jobview.usajobs.gov/GetJob.aspx?JobID=89528078.

Sackler Scholars in Biophysics

The University of Washington announces The Sackler Scholars Program in Integrative Biophysics, a new postdoctoral program in interdisciplinary biophysics research. This program will support outstanding young scientists conducting research at the intersection of medicine, biology and the physical sciences. The interface between physical and biological sciences is rapidly opening new frontiers in biomedical research. To advance this fertile research area in a highly effective manner, we have launched the inter-departmental Sackler Scholars Program. Laboratories across the entire University of Washington—the School of Medicine, the College of Engineering and the College of Arts and Sciences — are participating in this new initiative. The Sackler Scholars Program enables the brightest young scientists to combine the experimental and computational expertise of multiple laboratories to promote progress in biophysics research.

For more information about this exciting new program and the application process, go to our website: **http://depts.washington.edu/pbiopage/sackler/index.php**

The UW Sackler Scholars Program in Integrative Biophysics is made possible by a generous gift from the Raymond and Beverly Sackler Foundation.

The University of Washington is building a culturally diverse community and strongly encourages applications from women, minorities, individuals with disabilities and covered veterans. The University of Washington is an Equal Opportunity, Affirmative Action Employer.

Sandia National Laboratories

Harry S. Truman Research Fellowship
In National Security Science and Engineering

Sandia National Laboratories is one of the country's largest research facilities employing nearly 8,500 people at major facilities in Albuquerque, New Mexico and Livermore, California. Please visit our website at www.sandia.gov.

We are searching for outstanding Ph.D. candidates to apply for the Harry S. Truman Research Fellowship in National Security Science and Engineering. This initial one-year appointment may be extended, at management's discretion, for two additional one-year appointments. The salary is $110,800 per year. This position requires a United States Department of Energy security clearance, which requires United States citizenship.

The Truman Fellowship provides the opportunity for recipients to pursue independent research of their choosing that supports Sandia's national security mission. Candidates are expected to have solved a major scientific or engineering problem in their thesis work or will have provided a new approach or insight to a major problem, as evidenced by a recognized impact in their field.

Candidates must have a Ph.D. within the past 3 years, or will complete all Ph.D. requirements by commencement of appointment, with a broad-based background and extensive knowledge of research in one or more of the following areas: advanced computing, information systems and mathematics; cyber security; bioscience and technology; combustion, chemical and earth sciences; engineering sciences; geosciences; intelligent systems; materials science and technology; microelectronics and microsystems; nano sciences and technology; nuclear and alternative energy; pulsed power and directed energy; and remote sensing and satellite systems. Candidates must be seeking their first national laboratory appointment (pre postdoc internships excluded), have excellent academic (minimum 3.5 undergraduate and 3.7 graduate GPA preferred) and research qualifications, good communication skills, and enjoy working in a team-oriented, dynamic environment.

For complete application instructions, please visit:
http://www.sandia.gov/careers/fellowships.html#truman

Please submit the complete package to: Roberta Rivera, Sandia NationalLaboratories, P.O. Box 5800, MS 1497, Albuquerque, New Mexico 87185-1497, or email rjriver@sandia.gov, or fax 505-284-5950. Please reference: Job #635052. All materials must be received by December 5, 2010.

U.S. Citizenship Normally Required. Equal Opportunity Employer. M/F/D/V.

LOCKHEED MARTIN

POSITIONS OPEN

FACULTY POSITION
in Tumor Immunology

The Department of Medicine in conjunction with the Integrated Department of Immunology at National Jewish Health and the University of Colorado Denver is seeking a candidate to fill a position in tumor immunology at the **ASSISTANT** or **ASSOCIATE PROFESSOR** level in the newly created Thoracic Oncology Division at National Jewish Health, the leader in respiratory care as ranked by U.S. News and World Report.

Both departments enjoy a rich tradition of discovery and training in basic and translational pulmonary biology and immunology in a very collegial environment. We are seeking candidates pursuing innovative research in basic and/or translational tumor immunology, especially related to epithelial cell carcinoma and lung cancer, and who will bring novel technology and expertise to our institution. The applicant should have a Ph.D., M.D., or equivalent degree; a substantive record of publications in peer-reviewed journals; demonstrated interest in tumor immunology research, and the potential to develop a competitive independent research program. The ideal candidate would complement the existing areas of research and actively pursue collaborations with basic and clinical scientists.

Candidates will be expected to establish and maintain a strong extramurally funded research program and participate in teaching to graduate and medical students. Scientists with a record of achievement and commitment to excellence are encouraged to apply.

To apply, submit a cover letter, curriculum vitae, and a brief statement of current and future research interests, as well as names and contact information of three professional references to **e-mail: durans@njhealth.org.**

National Jewish Health and the University of Colorado Denver are committed to diversity and equality in employment.

ASSISTANT PROFESSOR
of Neuroscience

The School of Biological Sciences at Illinois State University (**website: http://www.bio.illinoisstate.edu**) invites applications for a tenure-track position in Cellular Neurophysiology. Candidates utilizing modern electrophysiological techniques are encouraged to apply. The area of research expertise is open; current neuroscience interests on campus include drugs of abuse, neurodegeneration, neuropharmacology, stroke, neuroimmune system interactions, behavioral economics, and behavioral neuroendocrinology. The new faculty will participate in the development of a Core Neuroscience Facility, and undergraduate and graduate sequences in neuroscience as part of a federally funded initiative. The primary teaching responsibility is in graduate neuroscience, with a rotation through undergraduate animal physiology. The successful candidate is expected to establish a competitive extramurally funded research program and to mentor B.S., M.S., and Ph.D. students. Postdoctoral experience required. Send cover letter, curriculum vitae, a brief statement of research goals, and contact information for three references as a single PDF file to: **Paul Garris, Neuroscience Search Committee, in c/o Sally Little** via **e-mail: salitt2@ilstu.edu** (mailing instructions on website). Review of applications will begin on October, 11, 2010, and continue until position is filled. Intended start date is August 16, 2011. *Illinois State University is an Equal Opportunity University encouraging diversity.*

MOLECULAR CARDIOLOGIST, ENDOWED CHAIR. The Molecular Cardiology Program at Weill Medical College of Cornell University seeks independent investigators as tenure-track or tenured faculty members. This position includes an endowed chair at the **ASSOCIATE PROFESSOR** or **PROFESSOR** rank. Successful candidates (M.D., M.D.-Ph.D., or Ph.D.) should have an established track record of extramural funding and will be provided with newly renovated research space and a generous startup package. Applicants should forward curriculum vitae, research plan, and three references to: **Voula Papoutsis, Search Committee, Division of Cardiology, Cornell Medical College, Starr 4, 525 East 68th Street, New York, NY 10021. Telephone: 212-746-2169. Fax: 212-746-6951. E-mail: stp2003@med.cornell.edu.** *Cornell is an Equal Opportunity Employer.*

TWO TENURE-TRACK FACULTY POSITIONS
Department of Biological Sciences
York College of Pennsylvania

The Department of Biological Sciences at York College of Pennsylvania is accepting applications for two full-time tenure-track positions beginning in August 2011 (**website: http://www.ycp.edu/1212.htm**). First position is in Molecular Biology with the primary responsibility for teaching the introductory Biology course for Biology and Allied Health majors and a molecular biology focused upper-level lecture and laboratory course. Second position is in Conservation Biology and/or Computational Biology and will be responsible for developing a course in Biostatistics for Biology majors. Ideal candidates will have a doctoral degree in Biology or related discipline that will augment existing departmental expertise. York College (**website: http://www.ycp.edu**) is a comprehensive college offering over 50 baccalaureate majors in the arts and sciences and in professional fields. The college has an enrollment of 4600 full-time and 800 part-time students. The campus is located in South-Central Pennsylvania (50 miles north of Baltimore, Maryland), and offers competitive salaries and fringe benefits. Candidates should send curriculum vitae, statement of teaching philosophy and research interests, graduate transcripts, and three letters of recommendation to: **Ron Kaltreider, Ph.D., Chair, Department of Biological Sciences, York College of Pennsylvania, 441 Country Club Road, York, PA 17403.** Review of applications will begin October 22, 2010, and deadline for submission is November 5, 2010. *York College is an Equal Opportunity Employer.* For a copy of York College's Annual Security Report, you may contact the Office of Campus Safety or view online at **website: http://www.ycp.edu/security/844.htm.**

GENERAL ADVERTISEMENT

The Department of Chemistry at the University of Michigan invites applications for an anticipated **TENURE-TRACK POSITION** at any rank in any subdiscipline of Chemistry with a proposed start date of September 1, 2011. This would be a University-year appointment (nine-month academic salary with summer salary supported by research funds). Candidates are expected to develop an internationally recognized program of scholarly research and to excel in teaching at undergraduate and graduate levels. Detailed information regarding the electronic application process and required materials is available online at (**website: https://www.chem.lsa.umich.edu/chem/facultyrecruit/**). The position will remain open until filled but preference will be given to applicants who have submitted all requested materials prior to October 15, 2010. Information about the Chemistry Department is available on the **website: http://www.umich.edu/~michchem.** Questions about the application process should be sent to **e-mail: chemfac10@umich.edu.** *Women and minorities are encouraged to apply. The University of Michigan is supportive of the needs of dual career couples and is an Equal Opportunity/Affirmative Action Employer.*

CHEMICAL ENGINEERING FACULTY POSITION

California Institute of Technology invites applications for a tenure-track faculty position in the Division of Chemistry and Chemical Engineering in the area of chemical engineering. Candidates with strong commitments to research and teaching excellence are encouraged to apply. We expect to make the appointment at the **ASSISTANT PROFESSOR** level, but consideration will be given to exceptionally well-qualified applicants at the **ASSOCIATE** and **FULL PROFESSOR** levels. Appointment will be contingent upon completion of all requirements for a Ph.D. in chemical engineering or in a related field. Submit curriculum vitae, publication list, a description of proposed research, and three letters of recommendation to: **Chair of the Chemical Engineering Search Committee, M/C 210-41, California Institute of Technology, Pasadena, CA 91125.** Submission should be made electronically to **e-mail: search@cheme.caltech.edu.** Applications should be received by October 15, 2010. *The California Institute of Technology is an Equal Opportunity/Affirmative Action Employer. Women, minorities, veterans, and disabled persons are encouraged to apply.*

ASSISTANT PROFESSOR
of Biochemistry

The Department of Chemistry and Biochemistry of the University of Arizona (UA), in conjunction with UA's Colleges of Science and Medicine, seeks applications from Ph.D. scientists for a tenure-eligible position in any area of modern biochemistry. The Department of Chemistry and Biochemistry was awarded in excess of $19 million in federal funding in 2008–09 and includes more than 45 faculty with broad research interests in the biological and chemical sciences. Laboratory space associated with the department includes the new Medical Research Building that houses interdisciplinary basic biomedical research groups from several colleges, and the new Chemical Sciences Building. The successful candidate will be offered a competitive start-up package and will teach in undergraduate, graduate, and/or medical curricula. To apply, please submit a letter of application, curriculum vitae, and statements of research and teaching interests online at **website: http://www.uacareertrack.com** (position **#43764**). Three letters of recommendation should be sent to: **Professor William Montfort, Biochemistry Faculty Search, c/o Beth Vinson, Department of Chemistry and Biochemistry, PO Box 210041, Tucson, AZ 85721.** Review of applications will begin October 15 and continue until the position is filled.

The University of Arizona is an Equal Employment Opportunity/Affirmative Action employer—Minorities/Women/Persons with Disabilities/Veterans. Women and minorities are especially encouraged to apply. The Immigration Reform and Control Act requires you to have proof of authorization to work in the United States.

NON-TENURE FACULTY POSITION
Department of Pathology at
Case Western Reserve University
School of Medicine

The Department of Pathology at Case Western Reserve University School of Medicine, invites applications for a non-tenure faculty position in prion disease research. The position requires expertise in protein chemistry, including the ability to carry out purification, immunoprecipitation, Western blot technique, and protein misfolding cyclic amplification (PMCA).

Desirable candidates will be expected to apply or adapt existing protocols. The ability to coordinate collaborations related to sharing materials, information and other data for publication is also expected. Contribution to the writing of research papers and reviews is desirable.

The Candidate is also expected to have skills in (1) managing database programs through Microsoft Access and Java and (2) following and monitoring quality control policies as necessary with BSL2 and BSL3 levels.

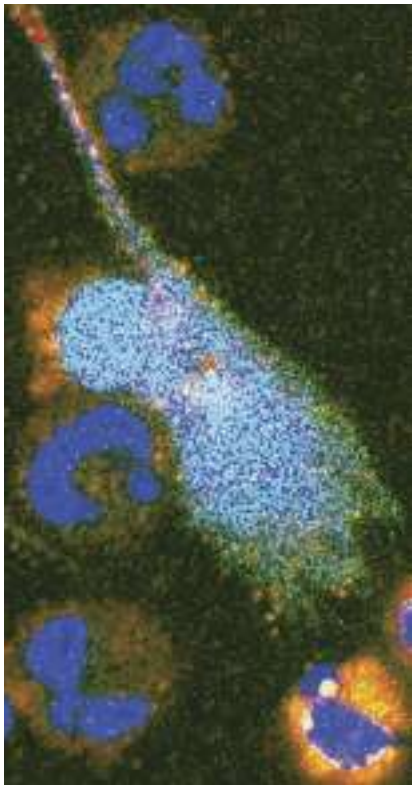
Appropriate candidates must have a Ph.D. in chemistry or biology.

Applicants should submit their curriculum vitae, a brief statement of research interests, copies of any publications, and at least three letters of reference to **e-mail: sab69@case.edu.**

BASIC SCIENCE DIVISION CHIEF

The Duke University Department of Anesthesiology is currently undergoing expansion of its basic science research program. We are recruiting a **SENIOR LEVEL SCIENTIST** to direct this growth. An endowed chair is available to support the successful candidate, in addition to receiving startup funds for the laboratory. The successful candidate will have an established record of NIH funding and mentoring. While the candidate will be expected to continue their own research, additional responsibilities will include faculty recruitment, integration of departmental basic science resources, planning and managing growth, and identifying opportunities for research training. The Department of Anesthesiology has existing strengths in acute CNS injury, pain neurobiology, mitochondrial dysfunction in sepsis, and cardiovascular genomic research upon which future growth can be based or supplemented. Candidates are requested to send inquiries and a current curriculum vitae or biosketch to **David S. Warner, M.D.** (**e-mail: david.warner@duke.edu**).

MEETINGS



Autoantibody binding to neutrophil extracellular traps
Image courtesy of Dwivedi and Radic, UTHSC.

GWEN KNAPP CENTER FOR LUPUS & IMMUNOLOGY RESEARCH and
THE SECTION OF RHEUMATOLOGY present

THE GWEN KNAPP SYMPOSIUM:

THE ANTIGEN TARGETS OF AUTOIMMUNE DISEASE

OCTOBER 8-9, 2010

THE UNIVERSITY OF CHICAGO
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Chicago, Illinois

KEYNOTE SPEAKER: IRUN COHEN, *WEIZMANN INSTITUTE*

SPEAKERS:

John Cambier, *National Jewish Medical and Research Center*
Steve Clarke, *University of North Carolina*
Keith Elkon, *University of Washington*
Loren Erikson, *University of Virginia*
Haochu Huang, *University of Chicago*
Greg Lemke, *Salk Institute*
Cliff Lowell, *University of California, San Francisco*
Marc Monestier, *Temple University School of Medicine*
Laurence Morel, *University of Florida*
Sylviane Muller, *CNRS, Strasbourg*
David Nemazee, *Scripps Research Institute*
Michel Nussenzweig, *Rockefeller University*
Paul Plotz, *National Institute of Health*
Bill Robinson, *Stanford University*
Ann Rothstein, *University Mass Medical School*
Eng Tan, Scripps *Research Institute*
Takeshi Tsubata, *Tokyo Medical and Dental Center*
PJ Utz, *Stanford University*
Thomas Winkler, *University of Erlangen*

Organizing Committee: **Marko Radic, Mark Shlomchik, Tammy Utset, and Martin Weigert**
For more information, please visit: http://knappcenter.uchicago.edu or email Angela Hayes ahayes@bsd.uchicago.edu

POSITIONS OPEN

★ **Institute for Defense Analyses** ★

For over half a century, the Institute for Defense Analyses has been successfully pursuing its mission to bring analytic objectivity and understanding to complex issues of national security. IDA is a not-for-profit corporation that provides scientific, technical and analytical studies to the Office of the Secretary of Defense, the Joint Chiefs of Staff, the Unified Commands and Defense Agencies as well as to the President's Office of Science and Technology Policy.

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• Pure & Applied Mathematics	• Mechanical	• Statistics
	• Systems	• Technology Policy

Along with competitive salaries, IDA provides excellent benefits including comprehensive health insurance, paid holidays, 3 week vacations and more – all in a professional and technically vibrant environment.

Applicants will be subject to a security investigation and must meet eligibility requirements for access to classified information. U.S. citizenship is required. IDA is proud to be an equal opportunity employer.

Please visit our website www.ida.org for more information on our opportunities.

IDA **Please submit applications to: http://www.ida.org/careers.php**

Institute for Defense Analyses 4850 Mark Center Drive Alexandria, VA 22311

POSITIONS OPEN

DIRECTOR POSITION
Description for the Institute for Advanced Cyber-Enabled Research at Michigan State University

Michigan State University (MSU) seeks a Director of the recently formed MSU Institute for Cyber-Enabled Research (iCER). Computational sciences and their underlying mathematical theories have become core methodologies in all areas of modern science. iCER aims at capitalizing on significant algorithmic advances and rapid progress in massively parallel computer architectures to employ large-scale computational approaches as a predictive research tool in a wide range of scientific disciplines. Candidates will be entertained in any discipline at Michigan State University included in the Colleges of Engineering, Natural Science, and Social Science. Additional information can be found on the iCER **website: http://www.icer.msu.edu.**

The successful candidate will be an internationally prominent, highly visible scholar who will lead the computational science efforts at MSU. The Director will report directly to the Vice President for Research and Graduate Studies. The Director will be empowered to build a high-profile research program in high-performance computing and/or computational science with an academic home in one or more departments. MSU is committed to further faculty hires in high performance computing and computational science and anticipates that the iCER director will take a leadership role in attracting high quality faculty, will interact with the current affiliated faculty, and will spearhead the development of large interdisciplinary programs to obtain major high-impact research grants. The iCER facility is located in newly renovated space on campus. There is support available for an associate director to manage day-to-day operations, a faculty scholars program, postdoctoral and visiting scholars, graduate students, and provisions for educational resources (courses, workshops, and seminars), and for training in the use of computational hardware and software. Facilities and resources associated with iCER include MSU's high-performance computing center (HPCC) that is on a continual upgrade path to make sure that MSU remains competitive as a University scale computing facility.

Application materials including curriculum vitae, research statement, and a list of four references should be submitted to the iCER search committee at **e-mail: vprgs@msu.edu.** Consideration of applications will commence September 1, 2010, and continue through November 30, 2010, or until the position is filled.

MSU is an Affirmative Action/Equal Opportunity Employer. MSU is committed to achieving excellence through cultural diversity. The university actively encourages applications and/or nominations of women, persons of color, veterans, and persons with disabilities.

WEILL CORNELL MEDICAL COLLEGE
The Methodist Hospital Research Institute

The Molecular Imaging Program of the Department of Radiology develops novel agents and new technologies to image molecular processes and treat diseases. The research focuses on cancer, cardiovascular disease, neurodegeneration, cell therapy, stem cell biology, gene therapy, and nanotechnology. In November 2010, our program will be moving into a brand new 440,000 square foot Methodist Hospital Research Institute building with open laboratory space design, core facilities to enhance interdisciplinary research, a Good Manufacturing Practice (GMP) facility to prepare clinical-grade imaging and therapeutic agents, state-of-the-art imaging equipment for preclinical studies, a cyclotron and hot cell facility and, a specialized laboratory for infectious disease research. The Molecular Imaging Program has created a number of new **POSTDOCTORAL FELLOW** and **RESEARCH ASSOCIATE** positions. Self-motivated scientists with expertise in liposomes, peptides, nanoparticles, radiochemistry, bioconjugation, MR physics, molecular biology and/or animal models are encouraged to apply and join our dynamic research team. Please e-mail curriculum vitae and contact information of three references to **Dr. Ching H. Tung** at **e-mail: ctung@tmhs.org.**

POSITIONS OPEN

ASSISTANT PROFESSOR
in Pharmacology

The Department of Basic Pharmaceutical Sciences in the School of Pharmacy at The University of Louisiana at Monroe (ULM) invites applications for a twelve-month tenure-track faculty position of Assistant Professor. This position includes an attractive recruitment package of salary, startup, and laboratory space. Candidates should have an earned doctorate in physiology or pharmacology and postdoctoral research experience, preferably in the areas of cancer biology, endocrinology, or neuroscience. The successful candidate is expected to develop an independent, externally funded research program, and contribute to teaching professional and graduate courses in the areas of physiology and pharmacology. Located in Monroe, a city whose metropolitan area population exceeds 100,000, the ULM campus offers a tranquil and cordial setting encompassing 238 acres, over 50 buildings, and an off-campus farm. Candidate screening will begin December 15, 2011, and candidate interviews will start soon afterwards and continue until the position is filled. Qualified individuals should submit their curriculum vitae, list of three references, and a statement of current interests and future goals emphasizing how their interests might complement the strengths of the Department to: **Dr. Paul W. Sylvester, Pharmacology Search Committee, College of Pharmacy, University of Louisiana at Monroe, 700 University Avenue, Monroe, LA 71209-0470. Email: sylvester@ulm.edu**. *The University of Louisiana at Monroe is an Equal Opportunity/Affirmative Action Employer.*

FACULTY POSITION
in Molecular, Cellular, and Developmental Biology University of Colorado at Boulder

The Department of Molecular, Cellular, and Developmental Biology invites applications for a tenure-track **ASSISTANT PROFESSOR** in the area of molecular, cellular, or developmental biology with an emphasis on basic molecular biological problems. Applicants must have a Ph.D., M.D., or equivalent in addition to postdoctoral research experience. The candidate is expected to develop a vigorous and innovative research program, and have enthusiasm for teaching at the undergraduate and graduate levels.

Review of applications will begin on November 1, 2010 and continue until the position is filled. Application materials are accepted electronically at **website: https://www.jobsatcu.com,** posting number **810875.** Applicants should submit a curriculum vitae and a concise statement of research and teaching interests, and arrange to have three reference letters sent.

For questions or concerns on submitting your materials electronically, please contact **e-mail: mcdbsrch@colorado.edu.**

See **website: http://www.colorado.edu/ArtsSciences/Jobs/** for full job description. *The University of Colorado at Boulder is committed to diversity and equality in education and employment.*

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Careers Forum
Science Careers
From the journal *Science* AAAS
www.ScienceCareers.org

POSITIONS OPEN

ASSISTANT PROFESSOR in GENETICS
Hendrix College

The Biology Department invites applications for a tenure-track position at the rank of Assistant Professor in genetics beginning in the fall of 2011. Geneticists of all specialties are encouraged to apply, especially those with interest in microbial genetics and/or bioinformatics. The college seeks to extend its tradition of excellence in teaching and scholarship by attracting faculty who combine mastery of their disciplines with broad intellectual interests and commitment to the aims of a liberal arts college. Development of an externally funded research program involving undergraduate students is expected and supported through appropriate course release. A doctorate or ABD at the time of appointment is required. Postdoctoral experience is welcomed but not required.

Applications should include a letter addressing the candidate's interest in teaching in a demanding but supportive liberal arts environment, curriculum vitae, teaching and research philosophy statements, three letters of recommendation (including the telephone numbers and e-mail addresses of the references), and graduate and undergraduate transcripts. Application materials should be sent to: **Dr. Matthew Moran, Chair, Department of Biology, Hendrix College, 1600 Washington Avenue, Conway, AR 72032.** Review of materials will begin on October 15 and continue until position is filled.

Hendrix College is a Phi Beta Kappa, Carnegie Baccalaureate institution, with an endowment of $145 million located in Conway, Arkansas, thirty miles from Little Rock. The College, affiliated with the United Methodist Church, has a strong commitment to excellence in teaching liberal arts. *Hendrix is an Equal Opportunity Employer. Women and members of minority groups are especially encouraged to apply.* Please visit our **website: http://www.hendrix.edu.**

NON-TENURED RESEARCH ASSISTANT PROFESSOR, RESEARCH ASSOCIATE, SENIOR POSTDOCTORAL FELLOW
Department Environmental and Occupational Health Graduate School Public Health University of Pittsburgh

Several positions are available in the laboratory of **Dr. Valerian E. Kagan** (Center for Free Radical and Antioxidant Biochemistry, Department of Environmental and Occupational Health, University of Pittsburgh). Candidates with interests in research on: (1) mass spectrometry/oxidative lipidomics/metabolomics, (2) mass-spectrometry and oxidative neurolipidomics, (3) lipid signaling in apoptosis and phagocytosis, (4) lipidomics of immune cells in cancer, or (5) mechanisms of nanoparticles interactions with cells in vitro and in vivo—are invited to apply. Participation in ongoing collaborations with laboratories in Sweden, Ireland, and Russia are possible. Candidates should have Ph.D. or M.D. with background in analytical biochemistry/chemistry, molecular/cell biology, redox biochemistry/biophysics or related fields. Experience with mass spectrometry of lipids and other small molecules, analytical chemistry/biochemistry as well as live cell (fluorescence) microscopy, immunoblotting, immunocytochemistry, and DNA transfection are desirable. Interested applicants should send curriculum vitae and names of three references to: **Dr. Valerian E. Kagan, e-mail: kagan@pitt.edu.** *University of Pittsburgh is an Equal Opportunity Employer.*

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